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☐ 1. Document ID: US 6180406 B1

L3: Entry 1 of 48 File: USPT Jan 30, 2001

US-PAT-NO: 6180406
DOCUMENT-IDENTIFIER: US 6180406 B1

TITLE: Methods for generating polynucleotides having desired characteristics by iterative selection and recombination

DATE-ISSUED: January 30, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Stemmer; Willem P.C.	Los Gatos	CA	N/A	N/A

US-CL-CURRENT: 435/440; 435/6, 435/91.2, 536/23.1, 536/24.3

ABSTRACT:

A method for DNA reassembly after random fragmentation, and its application to mutagenesis of nucleic acid sequences by in vitro or in vivo recombination is described. In particular, a method for the production of nucleic acid fragments or polynucleotides encoding mutant proteins is described. The present invention also relates to a method of repeated cycles of mutagenesis, shuffling and selection which allow for the directed molecular evolution in vitro or in vivo of proteins.

69 Claims, 37 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 37

L3: Entry 1 of 48 File: USPT Jan 30, 2001

DOCUMENT-IDENTIFIER: US 6180406 B1
TITLE: Methods for generating polynucleotides having desired characteristics by iterative selection and recombination

DRPR:
FIG. 20 schematically shows the generation of combinatorial libraires using synthetic or naturally-occurring intron sequences as the basis for recombining a plurality of exons species which can lack sequence identity (as exemplified by random sequence exons), wherein homologous and/or site-specific recombination occurs between intron sequences of distinct library members.

DEPR:
One variation involves the use of multiple binding targets (multiple epitope species, multiple receptor species), such that a scFv library can be simultaneously screened for a multiplicity of scFv which have different binding specificities. Given that the size of a scFv library often limits the diversity of potential scFv sequences, it is typically desirable to use scFv libraries of as large a size as possible. The time and economic considerations of generating a number of very large polysome scFv-display libraries can become prohibitive. To avoid this substantial problem, multiple predetermined epitope species (receptor species) can be concomitantly screened in a single library, or sequential screening against a number of epitope species can be used. In one variation, multiple target epitope species, each encoded on a separate bead (or subset of beads), can be mixed and incubated with a polysome-display scFv library under suitable binding conditions. The collection of beads, comprising multiple epitope species, can then be used to isolate, by affinity selection, scFv library members. Generally, subsequent affinity screening rounds can include the same mixture of beads, subsets thereof, or beads containing only one or two individual epitope species. This approach affords efficient screening, and is compatible with laboratory automation, batch processing, and high throughput screening methods.

☐ 2. Document ID: US 6171820 B1

L3: Entry 2 of 48 File: USPT Jan 9, 2001

US-PAT-NO: 6171820
DOCUMENT-IDENTIFIER: US 6171820 B1

TITLE: Saturation mutagenesis in directed evolution

DATE-ISSUED: January 9, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA	N/A	N/A

US-CL-CURRENT: 435/69.1; 435/69.7, 435/7.6, 530/350

ABSTRACT:

Disclosed is a rapid and facilitated method of producing from a parental template polynucleotide, a set of mutagenized progeny polynucleotides whereby at each original codon position there is produced at least one substitute codon encoding each of the 20 naturally encoded amino acids. Accordingly, there is also provided a method of producing from a parental template polypeptide, a set of mutagenized progeny polypeptides wherein each of the 20 naturally encoded amino acids is represented at each original amino acid position. The method provided is termed site-saturation mutagenesis, or simply saturation mutagenesis, and can be used in combination with other mutagenization processes, such as, for example, a process wherein two or more related polynucleotides are introduced into a suitable host cell such that a hybrid polynucleotide is generated by recombination and reductive reassortment. Also provided are vector and expression vehicles including such polynucleotides, polypeptides expressed by the hybrid polynucleotides and a method for screening for hybrid polypeptides.

13 Claims, 2 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 2

L3: Entry 2 of 48 File: USPT Jan 9, 2001

DOCUMENT-IDENTIFIER: US 6171820 B1
TITLE: Saturation mutagenesis in directed evolution

DEPR:
One variation involves the use of multiple binding targets (multiple epitope species, multiple receptor species), such that a scfv library can be simultaneously screened for a multiplicity of scfv which have different binding specificities. Given that the size of a scfv library often limits the diversity of potential scfv sequences, it is typically desirable to us scfv libraries of as large a size as possible. The time and economic considerations of generating a number of very large polysome scFv-display libraries can become prohibitive. To avoid this substantial problem, multiple predetermined epitope species (receptor species) can be concomitantly screened in a single library, or sequential screening against a number of epitope species can be used. In one variation, multiple target epitope species, each encoded on a separate bead (or subset of beads), can be mixed and incubated with a polysome-display scfv library under suitable binding conditions. The collection of beads, comprising multiple epitope species, can then be used to isolate, by affinity selection, scfv library members. Generally, subsequent affinity screening rounds can include the same mixture of beads, subsets thereof, or beads containing only one or two individual epitope species. This approach affords efficient screening, and is compatible with laboratory automation, batch processing, and high throughput screening methods.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 3. Document ID: US 6168919 B1

L3: Entry 3 of 48 File: USPT Jan 2, 2001

US-PAT-NO: 6168919
DOCUMENT-IDENTIFIER: US 6168919 B1

TITLE: Screening methods for enzymes and enzyme kits

DATE-ISSUED: January 2, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA	N/A	N/A

US-CL-CURRENT: 435/6; 435/183, 435/252.3, 435/320.1, 435/325, 435/4, 435/91.1, 435/91.4, 435/91.41, 536/23.1, 536/23.2, 536/23.4

ABSTRACT:

Recombinant enzyme libraries and kits where a plurality of enzymes are each characterized by different physical and/or chemical characteristics and classified by common characteristics. The characteristics are determined by screening of recombinant enzymes expressed by a DNA library produced from various microorganisms. Also disclosed is a process for identifying clones of a recombinant library which express a protein with a desired ctivity by screening a library of expression clones randomly produced from DNA of at least one microorganism, said screeing being effected on expression products of said clones to thereby identify clones which express a protein with a desired activity. Also disclosed is a process of screening clones having DNA from an uncultivated microorganism for a specified protein activity by screening for a specified protein activity in a library of clones prepared by (I) recovering DNA from a DNA population derived from at least one uncultivated microorganism; and (ii) transforming a host with recovered DNA to produce a library of clones which is screened for the specified protein activity.

9 Claims, 8 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 6

L3: Entry 3 of 48 File: USPT Jan 2, 2001

DOCUMENT-IDENTIFIER: US 6168919 B1
TITLE: Screening methods for enzymes and enzyme kits

CLPR:
1. A method for identifying clones of a recombinant library which express a protein with a desired characteristic, produced from DNA recovered from a plurality of species of organisms, comprising:

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

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☐ 4. Document ID: US 6165793 A

L3: Entry 4 of 48 File: USPT Dec 26, 2000

US-PAT-NO: 6165793
DOCUMENT-IDENTIFIER: US 6165793 A

TITLE: Methods for generating polynucleotides having desired characteristics by iterative selection and recombination

DATE-ISSUED: December 26, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Stemmer; Willem P. C.	Los Gatos	CA	N/A	N/A

US-CL-CURRENT: 435/440; 435/6, 536/23.1, 536/24.3

ABSTRACT:

A method for DNA reassembly after random fragmentation, and its application to mutagenesis of nucleic acid sequences by in vitro or in vivo recombination is described. In particular, a method for the production of nucleic acid fragments or polynucleotides encoding mutant proteins is described. The present invention also relates to a method of repeated cycles of mutagenesis, shuffling and selection which allow for the directed molecular evolution in vitro or in vivo of proteins.

62 Claims, 37 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 37

L3: Entry 4 of 48 File: USPT Dec 26, 2000

DOCUMENT-IDENTIFIER: US 6165793 A
TITLE: Methods for generating polynucleotides having desired characteristics by iterative selection and recombination

DRPR:
FIG. 20 schematically shows the generation of combinatorial libraries using synthetic or naturally-occurring intron sequences as the basis for recombining a plurality of exons species which can lack sequence identity (as exemplified by random sequence exons), wherein homologous and/or site-specific recombination occurs between intron sequences of distinct library members.

DEPR:
One variation involves the use of multiple binding targets (multiple epitope species, multiple receptor species), such that a scFv library can be simultaneously screened for a multiplicity of scFv which have different binding specificities. Given that the size of a scFv library often limits the diversity of potential scFv sequences, it is typically desirable to use scFv libraries of as large a size as possible. The time and economic considerations of generating a number of very large polysome scFv-display libraries can become prohibitive. To avoid this substantial problem, multiple predetermined epitope species (receptor species) can be concomitantly screened in a single library, or sequential screening against a number of epitope species can be used. In one variation, multiple target epitope species, each encoded on a separate bead (or subset of beads), can be mixed and incubated with a polysome-display scFv library under suitable binding conditions. The collection of beads, comprising multiple epitope species, can then be used to isolate, by affinity selection, scFv library members. Generally, subsequent affinity screening rounds can include the same mixture of beads, subsets thereof, or beads containing only one or two individual epitope species. This approach affords efficient screening, and is compatible with laboratory automation, batch processing, and high throughput screening methods.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 5. Document ID: US 6132970 A

L3: Entry 5 of 48 File: USPT Oct 17, 2000

US-PAT-NO: 6132970
DOCUMENT-IDENTIFIER: US 6132970 A

TITLE: Methods of shuffling polynucleotides

DATE-ISSUED: October 17, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Stemmer; Willem P. C.	Los Gatos	CA	N/A	N/A

US-CL-CURRENT: 435/6; 435/183, 435/69.1, 435/69.6, 435/91.2, 435/91.5, 536/23.1, 536/24.3

ABSTRACT:

The invention is directed to methods of shuffling polynucleotide variants. The methods entail conducting a multi-cyclic polynucleotide extension process on partially annealed polynucleotide strands having sequences from the plurality of chosen polynucleotide variants, the polynucleotide strands having regions of similarity and regions of heterology with each other and being partially annealed through the regions of similarity, under conditions whereby one strand serves as a template for extension of another strand with which it is partially annealed to generate a population of shuffled polynucleotides. Shuffled polynucleotides are then selected or screened to identify a shuffled polynucleotide having a desired functional property.

47 Claims, 15 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 15

L3: Entry 5 of 48 File: USPT Oct 17, 2000

DOCUMENT-IDENTIFIER: US 6132970 A
TITLE: Methods of shuffling polynucleotides

DEPR:
One variation involves the use of multiple binding targets (multiple epitope species, multiple receptor species), such that a scFv library can be simultaneously screened for a multiplicity of scFv which have different binding specificities. Given that the size of a scFv library often limits the diversity of potential scFv sequences, it is typically desirable to us scFv libraries of as large a size as possible. The time and economic considerations of generating a number of very large polysome scFv-display libraries can become prohibitive. To avoid this substantial problem, multiple predetermined epitope species (receptor species) can be concomitantly screened in a single library, or sequential screening against a number of epitope species can be used. In one variation, multiple target epitope species, each encoded on a separate bead (or subset of beads), can be mixed and incubated with a polysome-display scFv library under suitable binding conditions. The collection of beads, comprising multiple epitope species, can then be used to isolate, by affinity selection, scFv library members. Generally, subsequent affinity screening rounds can include the same mixture of beads, subsets thereof, or beads containing only one or two individual epitope species. This approach affords efficient screening, and is compatible with laboratory automation, batch processing, and high throughput screening methods.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 6. Document ID: US 6127190 A

L3: Entry 6 of 48 File: USPT Oct 3, 2000

US-PAT-NO: 6127190
DOCUMENT-IDENTIFIER: US 6127190 A

TITLE: Method for producing combinatorial libraries having a predetermined frequency of each species of test compound

DATE-ISSUED: October 3, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lebl; Michal	Oro Valley	AZ	N/A	N/A

US-CL-CURRENT: 436/518; 435/4, 435/6, 435/7.1, 435/DIG.49, 436/501, 436/528, 436/529, 436/530, 436/531, 436/543, 530/333 , 530/334, 536/18.5, 536/25.3

ABSTRACT:

A technique is disclosed for generating nonrandom combinatorial libraries on solid phase supports in which each of a set of predetermined species of test compounds is present on a predetermined number of solid phase supports, preferably on only one, and each solid phase support has only a single species of test compound. Each of the predetermined species of test compounds is prepared with absolute certainty because the technique does not employ any random division of the solid phase supports. Rather, the method is based on the stepwise division of a continuous solid phase support matrix prior to each synthetic step in which more than one type of subunit is added. Non-limiting examples of matrices of the solid phase supports include polypropylene membranes, polytetrafluoropropylene membranes and cotton thread. The combinatorial libraries made by the technique are also disclosed.

6 Claims, 3 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 3

L3: Entry 6 of 48 File: USPT Oct 3, 2000

DOCUMENT-IDENTIFIER: US 6127190 A
TITLE: Method for producing combinatorial libraries having a predetermined frequency of each species of test compound

BSPR:
The present invention concerns the field of combinatorial libraries of species of test compound that are synthesized on solid phase supports. A combinatorial library is a collection of multiple species of chemical compounds that consist of randomly selected subunits. Such libraries are useful because they can be screened to identify a ligand for an acceptor of interest. More particularly the invention concerns methods for constructing such libraries when the solid phase support is a material that can be readily fashioned into further divisible pieces.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 7. Document ID: US 6117679 A

L3: Entry 7 of 48 File: USPT Sep 12, 2000

US-PAT-NO: 6117679
DOCUMENT-IDENTIFIER: US 6117679 A

TITLE: Methods for generating polynucleotides having desired characteristics by iterative selection and recombination

DATE-ISSUED: September 12, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Stemmer; Willem P. C.	Los Gatos	CA	N/A	N/A

US-CL-CURRENT: 435/440; 435/6, 536/23.1, 536/24.3

ABSTRACT:

A method for DNA reassembly after random fragmentation, and its application to mutagenesis of nucleic acid sequences by in vitro or in vivo recombination is described. In particular, a method for the production of nucleic acid fragments or polynucleotides encoding mutant proteins is described. The present invention also relates to a method of repeated cycles of mutagenesis, shuffling and selection which allow for the directed molecular evolution in vitro or in vivo of proteins.

35 Claims, 72 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 37

L3: Entry 7 of 48 File: USPT Sep 12, 2000

DOCUMENT-IDENTIFIER: US 6117679 A
TITLE: Methods for generating polynucleotides having desired characteristics by iterative selection and recombination

DRPR:
FIG. 20 schematically shows the generation of combinatorial libraires using synthetic or naturally-occurring intron sequences as the basis for recombining a plurality of exons species which can lack sequence identity (as exemplified by random sequence exons), wherein homologous and/or site-specific recombination occurs between intron sequences of distinct library members.

DEPR:
One variation involves the use of multiple binding targets (multiple epitope species, multiple receptor species), such that a scFv library can be simultaneously screened for a multiplicity of scFv which have different binding specificities. Given that the size of a scFv library often limits the diversity of potential scFv sequences, it is typically desirable to use scFv libraries of as large a size as possible. The time and economic considerations of generating a number of very large polysome scFv-display libraries can become prohibitive. To avoid this substantial problem, multiple predetermined epitope species (receptor species) can be concomitantly screened in a single library, or sequential screening against a number of epitope species can be used. In one variation, multiple target epitope species, each encoded on a separate bead (or subset of beads), can be mixed and incubated with a polysome-display scFv library under suitable binding conditions. The collection of beads, comprising multiple epitope species, can then be used to isolate, by affinity selection, scFv library members. Generally, subsequent affinity screening rounds can include the same mixture of beads, subsets thereof, or beads containing only one or two individual epitope species. This approach affords efficient screening, and is compatible with laboratory automation, batch processing, and high throughput screening methods.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

8. Document ID: US 6060596 A

L3: Entry 8 of 48 File: USPT May 9, 2000

US-PAT-NO: 6060596
DOCUMENT-IDENTIFIER: US 6060596 A

TITLE: Encoded combinatorial chemical libraries

DATE-ISSUED: May 9, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lerner; Richard	La Jolla	CA	N/A	N/A
Janda; Kim	San Diego	CA	N/A	N/A
Brenner; Sydney	Edwards Passage	N/A	N/A	GBX

US-CL-CURRENT: 536/25.3

ABSTRACT:

The present invention describes an encoded combinatorial chemical library comprised of a plurality of bifunctional molecules having both a chemical polymer and an identifier oligonucleotide sequence that defines the structure of the chemical polymer. Also described are the bifunctional molecules of the library, and methods of using the library to identify chemical structures within the library that bind to biologically active molecules in preselected binding interactions.

17 Claims, 2 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 2

L3: Entry 8 of 48 File: USPT May 9, 2000

DOCUMENT-IDENTIFIER: US 6060596 A
TITLE: Encoded combinatorial chemical libraries

BSPR:
In another embodiment, the invention contemplates a library comprising a plurality of species of bifunctional molecules, thereby forming a repertoire of chemical diversity.

DEPR:
An encoded combinatorial chemical library is a composition comprising a plurality of species of bifunctional molecules that each define a different chemical structure and that each contain a unique identifier oligonucleotide whose nucleotide sequence defines the corresponding chemical structure.

DEPR:
A library of this invention is a repertoire of chemical diversity comprising a plurality of species of bifunctional molecules according to the present invention. The plurality of species in a library defines a family of chemical diversity whose species each have a different chemical moiety. Thus the library can define a family of peptides, lipids, oligosaccarides or any of the other classes of chemical polymers recited previously.

DEPR:
The number of different species in a library represents the complexity of a library and is defined by the polymer length of the chemical moiety, and by the size of the chemical unit alphabet that can be used to build the chemical unit polymer. The number of different species referred to by the phrase "plurality of species" in a library can be defined by the formula V.sup.a, i.e., V to power of a (exponent a). V represents the alphabet size, i.e., the number of different chemical units X available for use in the chemical moiety. "a" is an exponent to V and represents the number of chemical units of X forming the polymer A, i.e., the length of polymer A.

CLPR:
10. A library comprising a plurality of species of bifunctional molecules according to claim 1.

CLPR:
11. The library of claim 10 wherein said plurality of species is defined by the formula V.sup.a, where V represents the number of different chemical units forming an alphabet of possible chemical units of X, and a is an exponent to V and represents the number of chemical units of X forming polymer A.

☐ 9. Document ID: US 6007989 A

L3: Entry 9 of 48 File: USPT Dec 28, 1999

US-PAT-NO: 6007989
DOCUMENT-IDENTIFIER: US 6007989 A

TITLE: Methods of screening for compounds that derepress or increase telomerase activity

DATE-ISSUED: December 28, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
West; Michael D.	San Carlos	CA	N/A	N/A
Harley; Calvin B.	Palo Alto	CA	N/A	N/A
Weinrich; Scott L.	San Francisco	CA	N/A	N/A
Strahl; Catherine M.	San Francisco	CA	N/A	N/A
McEachern; Michael J.	San Francisco	CA	N/A	N/A
Shay; Jerry	Dallas	TX	N/A	N/A
Wright; Woodring E.	Arlington	TX	N/A	N/A
Blackburn; Elizabeth H.	San Francisco	CA	N/A	N/A
Kim; Nam Woo	Sunnyvale	CA	N/A	N/A
Vaziri; Homayoun	Toronto	N/A	N/A	CAX

US-CL-CURRENT: 435/6; 435/15, 435/375, 435/4, 435/7.2, 435/91.1, 435/91.2

ABSTRACT:

Method and compositions are provided for the determination of telomere length and telomerase activity, as well as the ability to increase or decrease telomerase activity in the treatment of proliferative diseases. Particularly, primers are elongated under conditions which minimize interference from other genomic sequences, so as to obtain accurate determinations of telomeric length or telomerase activity. In addition, compositions are provided for intracellular inhibition of telomerase activity and means are shown for slowing or reversing the loss of telomeric repeats in aging cells.

28 Claims, 43 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 43

L3: Entry 9 of 48 File: USPT Dec 28, 1999

DOCUMENT-IDENTIFIER: US 6007989 A
TITLE: Methods of screening for compounds that derepress or increase telomerase activity

DRPR:
FIG. 30 shows sequences of telomeric repeats from several budding yeast species. Specifically, telomere-enriched libraries were constructed from genomic DNA by standard methods. Uncut yeast genomic DNA was ligated to a blunt-ended linearized plasmid vector and then this ligated mix was digested with a restriction enzyme that cleaves both within the vector's polylinker and within a few kilobases of at least some of the putative telomeric ends of the species in question. No enzymatic pre-treatment was done to produce blunt-ends of the telomeres in the genomic DNA prior to the initial ligations. Plasmids were then recircularized with T4DNA ligase, and transformed into E. coli cells prior to screening for putative telomere clones by colony hybridization. The libraries from C. maltosa, C. pseudotropicalis, two strains of C. tropicalis, and K. lactis ATCC 32143, species which showed multiple bands that cross hybridized to the C. albicans telomeric repeat probe, were screened with this probe. A cloned S. cerevisiae telomere probe (repeat unit TG.sub.2-3 (GT).sub.1-3,) was used to screen the telomere--enriched library from C. glabrata, whose genomic DNA cross--hybridized with this, but not with the C. albicans telomeric repeat probe. C. guillermondii DNA did not appreciably cross-hybridize with either the C. albicans or the S. cerevisiae telomeric probes at the stringencies tested. The telomere--enriched library from this species was screened using total genomic C. guillermondii DNA as a probe. This procedure can be used to identify all clones containing repetitive sequences and we reasoned that telomeres should be a reasonable percentage of the repetitive sequences found in telomere enriched libraries. Typically, a few hundred E. coli transformants were obtained for each small library and up to nine putative telomere clones were obtained from each. Nine repetitive DNA clones were obtained from C. guillermondii, three of which proved to be telomeric.

☐ 10. Document ID: US 6004788 A

L3: Entry 10 of 48 File: USPT Dec 21, 1999

US-PAT-NO: 6004788
DOCUMENT-IDENTIFIER: US 6004788 A

TITLE: Enzyme kits and libraries

DATE-ISSUED: December 21, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA	N/A	N/A

US-CL-CURRENT: 435/183; 435/189, 435/190, 435/191, 435/193, 435/194, 435/195, 435/212, 435/232, 435/4

ABSTRACT:

Recombinant enzyme libraries and kits where a plurality of enzymes are each characterized by different physical and/or chemical characteristics and classified by common characteristics. The characteristics are determined by screening of recombinant enzymes expressed by a DNA library produced from various microorganisms.

2 Claims, 4 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 4

L3: Entry 10 of 48 File: USPT Dec 21, 1999

DOCUMENT-IDENTIFIER: US 6004788 A
TITLE: Enzyme kits and libraries

CLPR:
1. A kit comprising at least one container containing a mixture of enzymes, wherein said enzymes are obtained by culturing a gene expression library, comprising a pool of expression constructs, each expression construct comprising a vector containing one or more cDNA or genomic DNA fragments, wherein the cDNA or genomic DNA fragments in the pool of expression constructs are derived from a plurality of species of uncultured donor microorganisms, and wherein the cDNA or genomic DNA fagments are each operably-associated with one or more regulatory regions that drives expression of genes encoded by the cDNA or genomic DNA fragments in an appropriate host organism, wherein the enzyme is selected from the group consisting of oxidoreductase, transferase, hydrolase, lyase, isomerase, and ligase activity.

☐ 11. Document ID: US 5965408 A

L3: Entry 11 of 48 File: USPT Oct 12, 1999

US-PAT-NO: 5965408
DOCUMENT-IDENTIFIER: US 5965408 A

TITLE: Method of DNA reassembly by interrupting synthesis

DATE-ISSUED: October 12, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA	N/A	N/A

US-CL-CURRENT: 435/91.1; 435/183, 435/6, 435/91.2, 436/501, 530/350, 536/23.1, 536/24.3, 536/24.33

ABSTRACT:

Disclosed is a process of performing Sexual PCR which includes generating random polynucleotides by interrupting or blocking a synthesis or amplification process to show or halt synthesis or amplification of at least one polynucleotide, optionally amplifying the polynucleotides, and reannealing the polynucleotides to produce random mutant polynucleotides. Also provided are vector and expression vehicles including such mutant polynucleotides, polypeptides expressed by the mutant polynucleotides and a method for producing random mutant polypeptides.

14 Claims, 2 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 6

L3: Entry 11 of 48 File: USPT Oct 12, 1999

DOCUMENT-IDENTIFIER: US 5965408 A
TITLE: Method of DNA reassembly by interrupting synthesis

DEPR:
One variation involves the use of multiple binding targets (multiple epitope species, multiple receptor species), such that a scfv library can be simultaneously screened for a multiplicity of scfv which have different binding specificities. Given that the size of a scfv library often limits the diversity of potential scfv sequences, it is typically desirable to us scfv libraries of as large a size as possible. The time and economic considerations of generating a number of very large polysome scFv-display libraries can become prohibitive. To avoid this substantial problem, multiple predetermined epitope species (receptor species) can be concomitantly screened in a single library, or sequential screening against a number of epitope species can be used. In one variation, multiple target epitope species, each encoded on a separate bead (or subset of beads), can be mixed and incubated with a polysome-display scfv library under suitable binding conditions. The collection of beads, comprising multiple epitope species, can then be used to isolate, by affinity selection, scfv library members. Generally, subsequent affinity screening rounds can include the same mixture of beads, subsets thereof, or beads containing only one or two individual epitope species. This approach affords efficient screening, and is compatible with laboratory automation, batch processing, and high throughput screening methods.

☐ 12. Document ID: US 5966712 A

L3: Entry 12 of 48 File: USPT Oct 12, 1999

US-PAT-NO: 5966712
DOCUMENT-IDENTIFIER: US 5966712 A

TITLE: Database and system for storing, comparing and displaying genomic information

DATE-ISSUED: October 12, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Sabatini; Cathryn E.	San Jose	CA	N/A	N/A
Heath; Joe Don	Sunnyvale	CA	N/A	N/A
Covitz; Peter A.	San Francisco	CA	N/A	N/A
Klingler; Tod M.	Palo Alto	CA	N/A	N/A
Russo; Frank D.	Redwood City	CA	N/A	N/A
Berry; Stephanie F.	Fremont	CA	N/A	N/A

US-CL-CURRENT: 707/104; 435/6, 707/10

ABSTRACT:

Disclosed is a relational database system for storing and manipulating biomolecular sequence information, the database including genomic libraries for a plurality of types of organisms, the libraries having multiple genomic sequences, at least some of which represent open reading frames located along a contiguous sequence on each the plurality of organisms' genomes, and a user interface capable of receiving a selection of two or more of the genomic libraries for comparison and displaying the results of the comparison. The system also provides a user interface capable of receiving a selection of one or more probe open reading frames for use in determining homologous matches between such probe open reading frame(s) and the open reading frames in the genomic libraries, and displaying the results of the determination.

44 Claims, 34 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 41

L3: Entry 12 of 48 File: USPT Oct 12, 1999

DOCUMENT-IDENTIFIER: US 5966712 A
TITLE: Database and system for storing, comparing and displaying genomic information

ABPL:
Disclosed is a relational database system for storing and manipulating biomolecular sequence information, the database including genomic libraries for a plurality of types of organisms, the libraries having multiple genomic sequences, at least some of which represent open reading frames located along a contiguous sequence on each the plurality of organisms' genomes, and a user interface capable of receiving a selection of two or more of the genomic libraries for comparison and displaying the results of the comparison. The system also provides a user interface capable of receiving a selection of one or more probe open reading frames for use in determining homologous matches between such probe open reading frame(s) and the open reading frames in the genomic libraries, and displaying the results of the determination.

BSPR:
The invention further provides a computer system including a database containing genomic libraries for different types of organisms, which libraries have multiple genomic sequences, at least some of which representing open reading frames located along one or more contiguous sequences on each the organisms' genomes. The system also includes a user interface capable of receiving a selection of two or more genomic libraries for comparison and displaying the results of the comparison.

BSPR:

The invention also provides a computer system including a database including genomic libraries for one or more types of organisms, which libraries have multiple genomic sequences, at least some of which represent open reading frames located along one or more contiguous sequences on each the organisms' genomes. The system also includes a user interface capable of receiving a selection of one or more probe sequences for use in determining homologous matches between one or more probe sequences and the sequences in the genomic libraries, and displaying the results of the determination.

BSPR:
The invention further provides a method of presenting the genetic complement of an organism. The method involves providing a database including sequence libraries for a plurality of types of organisms, where the libraries have multiple biomolecular sequences, at least some of which represent open reading frames located along one or more contiguous sequences on each of the organisms' genomes. The methof further involves receiving a selection of one of the sequence libraries, determining open reading frames within the selected sequence library, and displaying the results as one or more unique identifiers for groups of related opening reading frames.

CLPR:
36. A computer program product comprising a computer-usable medium having computer-readable program code embodied thereon relating to a database including genomic libraries for one or more types of organisms, said libraries having multiple genomic sequences, at least some of which represent open reading frames located along one or more contiguous sequences on each the one or more organisms' genomes, the computer program product comprising computer-readable program code for effecting the following steps within a computing system:

CLPR:
39. A computer program product comprising a computer-usable medium having computer-readable program code embodied thereon relating to a database including genomic libraries for one or more types of organisms, said libraries having multiple genomic sequences, at least some of which represent open reading frames located along one or more contiguous sequences on each the one or more organisms' genomes, the computer program product comprising computer-readable program code for effecting the following steps within a computing system:

CLPV:
providing a database including sequence libraries for a plurality of types of organisms, said libraries having multiple biomolecular sequences, at least some of which represent open reading frames located along one or more contiguous sequences on each of the plurality of organisms' genomes;

CLPV:
providing a database including genomic libraries for a plurality of types of organisms, said libraries having multiple genomic sequences, at least some of which represent at least portions of open reading frames located along one or more contiguous sequences on each of the plurality of organisms' genomes;

CLPV:
providing a database including genomic libraries for a plurality of types of organisms, said libraries having multiple genomic sequences, at least some of which represent open reading frames located along one or more contiguous sequences on each the plurality of organisms' genomes;

CLPV:
providing a database including genomic libraries for a plurality of types of organisms, said libraries having multiple genomic sequences, at least some of which represent open reading frames located along one or more contiguous sequences on each the plurality of organisms' genomes;

CLPV:
a database including genomic libraries for a plurality of types of organisms, said libraries having multiple genomic sequences, at least some of which represent open reading frames located along one or more contiguous sequences on each the plurality of organisms' genomes; and

CLPV:

providing a database including genomic libraries for one or more types of organisms, said libraries having multiple genomic sequences, at least some of which represent open reading frames located along one or more contiguous sequences on each the one or more organisms' genomes;

CLPV:
a database including genomic libraries for one or more types of organisms, said libraries having multiple genomic sequences, at least some of which represent open reading frames located along one or more contiguous sequences on each the plurality of organisms' genomes;

CLPV:
providing a database including sequence libraries for a plurality of types of organisms, said libraries having multiple biomolecular sequences, at least some of which represent open reading frames located along one or more contiguous sequences on each of the plurality of organisms' genomes;

☐ 13. Document ID: US 5958672 A

L3: Entry 13 of 48 File: USPT Sep 28, 1999

US-PAT-NO: 5958672
DOCUMENT-IDENTIFIER: US 5958672 A

TITLE: Protein activity screening of clones having DNA from uncultivated microorganisms

DATE-ISSUED: September 28, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA	N/A	N/A

US-CL-CURRENT: 435/4; 435/183, 435/69.1, 536/23.1, 536/23.2

ABSTRACT:

Disclosed is a process of screening clones having DNA from an uncultivated microorganism for a specified protein, e.g. enzyme, activity by screening for a specified protein, e.g. enzyme, activity in a library of clones prepared by (i) recovering DNA from a DNA population derived from at least one uncultivated microorganism; and (ii) transforming a host with recovered DNA to produce a library of clones which is screened for the specified protein, e.g. enzyme, activity.

15 Claims, 5 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 5

L3: Entry 13 of 48 File: USPT Sep 28, 1999

DOCUMENT-IDENTIFIER: US 5958672 A
TITLE: Protein activity screening of clones having DNA from uncultivated microorganisms

CLPV:
culturing a gene expression library comprising a pool of expression constructs, each expression construct comprising a vector containing one or more cDNA or genomic DNA fragments, wherein the cDNA or genomic DNA fragments in the pool of expression constructs are derived from a plurality of species of donor organisms, and wherein the cDNA or genomic DNA fragments are each operably-associated with one or more regulatory regions that drives expression of genes encoded by the cDNA or genomic DNA fragments in an appropriate host organism; and

CLPV:
culturing a gene expression library, comprising a pool of expression constructs, each expression construct comprising a vector containing one or more cDNA or genomic DNA fragments, wherein the cDNA or genomic DNA fragments in the pool of expression constructs are derived from a plurality of species of donor microorganisms, and wherein the cDNA or genomic DNA fragments are each operably-associated with one or more regulatory regions that drives expression of genes encoded by the cDNA or genomic DNA fragments in an appropriate host organism; and

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☐ 14. Document ID: US 5955341 A

L3: Entry 14 of 48 File: USPT Sep 21, 1999

US-PAT-NO: 5955341
DOCUMENT-IDENTIFIER: US 5955341 A

TITLE: Heterodimeric receptor libraries using phagemids

DATE-ISSUED: September 21, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kang; Angray	La Jolla	CA	N/A	N/A
Barbas; Carlos	La Jolla	CA	N/A	N/A
Lerner; Richard	La Jolla	CA	N/A	N/A

US-CL-CURRENT: 435/235.1; 435/320.1, 530/387.3

ABSTRACT:

Filamentous phage comprising a matrix of cpVIII proteins encapsulating a genome encoding first and second polypeptides of an autogenously assembling receptor, such as an antibody, and a receptor comprised of the first and second polypeptides surface-integrated into the matrix via a cpVIII membrane anchor domain fused to at least on of the polypeptides.

10 Claims, 16 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 11

L3: Entry 14 of 48 File: USPT Sep 21, 1999

DOCUMENT-IDENTIFIER: US 5955341 A
TITLE: Heterodimeric receptor libraries using phagemids

DEPR:
The use of the above particle segregation methods provides a means for screening a population of filamentous phage particles present in a phage library of this invention. As applied to a phage library, screening can be utilized to enrich the library for one or more particles that express a heterodimer having a preselected ligand binding specificity. Where the library is designed to contain multiple species of heterodimers that all have some detectable measure of ligand binding activity, but differ in protein structure, antigenicity, ligand binding affinity or avidity, and the like, the screening methods can be utilized sequentially to first produce a library enriched for a preselected binding specificity, and then to produce a second library further enriched by further screening comprising one or more isolated phage particles. Methods for measuring ligand binding activities, antigenicity and the like interactions between a ligand and a receptor are generally well known and are not discussed further as they are not essential features of the present invention.

☐ 15. Document ID: US 5922545 A

L3: Entry 15 of 48 File: USPT Jul 13, 1999

US-PAT-NO: 5922545
DOCUMENT-IDENTIFIER: US 5922545 A

TITLE: In vitro peptide and antibody display libraries

DATE-ISSUED: July 13, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Mattheakis; Larry C.	Cupertino	CA	N/A	N/A
Dower; William J.	Menlo Park	CA	N/A	N/A

US-CL-CURRENT: 435/6; 435/5, 435/7.1, 436/518

ABSTRACT:

Improved methods and novel compositions for identifying peptides and single-chain antibodies that bind to predetermined receptors or epitopes. Such peptides and antibodies are identified by improved and novel methods for affinity screening of polysomes displaying nascent peptides.

4 Claims, 11 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 8

L3: Entry 15 of 48 File: USPT Jul 13, 1999

DOCUMENT-IDENTIFIER: US 5922545 A
TITLE: In vitro peptide and antibody display libraries

DEPR:
One variation involves the use of multiple binding targets (multiple epitope species, multiple receptor species), such that a polysome scFv library can be simultaneously screened for a multiplicity of scFv which have different binding specificities. Given that the size of a scfv library often limits the diversity of potential scFv sequences, it is typically desirable to use scFv libraries of as large a size as possible. The time and economic considerations of generating a number of very large polysome scFv-display libraries can become prohibitive. To avoid this substantial problem, multiple predetermined epitope species (receptor species) can be concomitantly screened in a single library, or sequential screening against a number of epitope species can be used. In one variation, multiple target epitope species, each encoded on a separate bead (or subset of beads), can be mixed and incubated with a polysome-display scFv library under suitable binding conditions. The collection of beads, comprising multiple epitope species, can then be used to isolate, by affinity selection, scfv library members. Generally, subsequent affinity screening rounds can include the same mixture of beads, subsets thereof, or beads containing only one or two individual epitope species. This approach affords efficient screening, and is compatible with laboratory automation, batch processing, and high throughput screening methods.

☐ 16. Document ID: US 5858731 A

L3: Entry 16 of 48 File: USPT Jan 12, 1999

US-PAT-NO: 5858731
DOCUMENT-IDENTIFIER: US 5858731 A

TITLE: Oligonucleotide libraries useful for producing primers

DATE-ISSUED: January 12, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Sorge; Joseph A.	San Diego	CA	N/A	N/A
Shoemaker; Daniel Davis	Stanford	CA	N/A	N/A

US-CL-CURRENT: 435/91.1; 536/24.3, 536/24.33, 536/25.3

ABSTRACT:

An oligonucleotide library is described that is1 useful for producing an oligonucleotide of preselected sequence comprising a plurality of oligonucleotide members comprising one or more oligonucleotide species and having the compositional formula (X).sub.a (N).sub.b ; wherein X represents a non-degenerate nucleotide base and N represents a degenerate nucleotide base; "a" represents the number of non-degenerate nucleotide positions and is from 3 to 8; "b" represents the number of degenerate nucleotide positions and is from 0 to 4 but not greater that "a"; and wherein each of the oligonucleotide species is capable of forming a hybridization complex with at least one other of the oligonucleotide species in the library such that a single ligation event of the hybridization complex with another hybridization complex derived from the library produces a ligation reaction product comprising greater than 12 contiguous nucleotide base pairs.

20 Claims, 7 Drawing figures Exemplary Claim Number: 14
Number of Drawing Sheets: 6

L3: Entry 16 of 48 File: USPT Jan 12, 1999

DOCUMENT-IDENTIFIER: US 5858731 A
TITLE: Oligonucleotide libraries useful for producing primers

BSPR:
In accordance with a related embodiment of the invention, library size limitations are overcome by the use of degenerate oligonucleotides in which a single oligonucleotide composition contains multiple oligonucleotide species. For example, a representative degenerate octanucleotide composition can be described by the formula 5'-XXNXXNXX-3', where nucleotides (or analogs thereof) designated "X" are the same at any one position for all octanucleotides in the composition (non-degenerate) and nucleotides designated "N" can be any one of A, T, G, C, and preferably a mixture of all four, or analogs thereof (degenerate).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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☐ 17. Document ID: US 5840485 A

L3: Entry 17 of 48 File: USPT Nov 24, 1998

US-PAT-NO: 5840485
DOCUMENT-IDENTIFIER: US 5840485 A

TITLE: Topologically segregated, encoded solid phase libraries

DATE-ISSUED: November 24, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lebl; Michal	Oro Valley	AZ	N/A	N/A
Lam; Kit S.	Tucson	AZ	N/A	N/A
Salmon; Sydney E.	Tucson	AZ	N/A	N/A
Krchnak; Victor	Oro Valley	AZ	N/A	N/A
Sepetov; Nikolai	Oro Valley	AZ	N/A	N/A
Kocis; Peter	Oro Valley	AZ	N/A	N/A

US-CL-CURRENT: 435/6; 435/7.1, 435/DIG.22, 435/DIG.34, 435/DIG.35, 435/DIG.38, 436/518, 530/300, 530/323, 536/23.1

ABSTRACT:

The invention relates to libraries of synthetic test compound attached to separate phase synthesis supports that also contain coding molecules that encode the structure of the synthetic test compound. The molecules may be polymers or multiple nonpolymeric molecules. The synthetic test compound can have backbone structures with linkages such as amide, urea, carbamate (i.e., urethane), ester, amino, sulfide, disulfide, or carbon-carbon, such as alkane and alkene, or any combination thereof. Examples of subunits suited for the different linkage chemistries are provided. The synthetic test compound can also be molecular scaffolds, such as derivatives of monocyclic of bicyclic carbohydrates, steroids, sugars, heterocyclic structures, polyaromatic structures, or other structures capable of acting as a scaffolding. Examples of suitable molecular scaffolds are provided. The invention also relates to methods of synthesizing such libraries and the use of such libraries to identify and characterize molecules of interest from among the library of synthetic test compound.

47 Claims, 13 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 8

L3: Entry 17 of 48 File: USPT Nov 24, 1998

DOCUMENT-IDENTIFIER: US 5840485 A
TITLE: Topologically segregated, encoded solid phase libraries

CLPR:
13. The library of claim 1 in which, on each said support, the structure of the test compound is encoded by a plurality of species of coding molecules.

CLPR:
16. The library of claim 14 in which the sequence of subunits of the test compound is encoded by a plurality of species of coding molecules.

CLPR:
19. The library of claim 17 in which the sequence of subunits of the test compound is encoded by a plurality of species of coding molecules.

CLPR:
41. The library of claim 32 in which, on each said support, the structure of the test compound is encoded by a plurality of species of coding molecules.

☐ 18. Document ID: US 5830644 A

L3: Entry 18 of 48 File: USPT Nov 3, 1998

US-PAT-NO: 5830644
DOCUMENT-IDENTIFIER: US 5830644 A

TITLE: Method for screening for agents which increase telomerase activity in a cell

DATE-ISSUED: November 3, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
West; Michael D.	San Carlos	CA	N/A	N/A
Shay; Jerry	Dallas	TX	N/A	N/A
Wright; Woodring E.	Arlington	TX	N/A	N/A

US-CL-CURRENT: 435/6; 435/15, 435/4, 435/7.2, 435/91.2, 436/34, 436/501, 436/63, 436/64, 436/94

ABSTRACT:

Method and compositions are provided for the determination of telomere length and telomerase activity, as well as the ability to increase or decrease telomerase activity in the treatment of proliferative diseases. Particularly, primers are elongated under conditions which minimize interference from other genomic sequences, so as to obtain accurate determinations of telomeric length or telomerase activity. In addition, compositions are provided for intracellular inhibition of telomerase activity and means are shown for slowing or reversing the loss of telomeric repeats in aging cells.

10 Claims, 54 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 42

L3: Entry 18 of 48 File: USPT Nov 3, 1998

DOCUMENT-IDENTIFIER: US 5830644 A
TITLE: Method for screening for agents which increase telomerase activity in a cell

DRPR:
FIG. 30 shows sequences of telomeric repeats from several budding yeast species. Specifically, telomere-enriched libraries were constructed from genomic DNA by standard methods. Uncut yeast genomic DNA was ligated to a blunt-ended linearized plasmid vector and then this ligated mix was digested with a restriction enzyme that cleaves both within the vector's polylinker and within a few kilobases of at least some of the putative telomeric ends of the species in question. No enzymatic pre-treatment was done to produce blunt-ends of the telomeres in the genomic DNA prior to the initial ligations. Plasmids were then recircularized with T4DNA ligase, and transformed into E. coli cells prior to screening for putative telomere clones by colony hybridization. The libraries from C. maltosa, C. pseudotropicalis, two strains of C. tropicalis, and K. lactis ATCC 32143, species which showed multiple bands that cross hybridized to the C. albicans telomeric repeat probe, were screened with this probe. A cloned S. cerevisiae telomere probe (repeat unit TG.sub.2-3 (GT).sub.1-3,) was used to screen the telomere--enriched library from C. glabrata, whose genomic DNA cross--hybridized with this, but not with the C. albicans telomeric repeat probe. C. quillermondii DNA did not appreciably cross-hybridize with either the C. albicans or the S. cerevisiae telomeric probes at the stringencies tested. The telomere-enriched library from this species was screened using total genomic C. guillermondii DNA as a probe. This procedure can be used to identify all clones containing repetitive sequences and we reasoned that telomeres should be a reasonable percentage of the repetitive sequences found in telomere enriched libraries. Typically, a few hundred E. coli transformants were obtained for each small library and up to nine putative telomere clones were obtained from each. Nine repetitive DNA clones were obtained from C. guillermondii, three of which proved to be telomeric.

☐ 19. Document ID: US 5830721 A

L3: Entry 19 of 48 File: USPT Nov 3, 1998

US-PAT-NO: 5830721
DOCUMENT-IDENTIFIER: US 5830721 A

TITLE: DNA mutagenesis by random fragmentation and reassembly

DATE-ISSUED: November 3, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Stemmer; Willem P. C.	Los Gatos	CA	N/A	N/A
Crameri; Andreas	Mountain View	CA	N/A	N/A

US-CL-CURRENT: 435/489; 435/6, 435/91.2

ABSTRACT:

A method for generating libraries of displayed peptides and/or antibodies (Abs) suitable for affinity interaction screening or phenotypic screening comprising: (i) obtaining selected library members comprising a displayed peptide and/or Ab and the corressponding polynucleotide (PN), or copies of it, (ii) pooling and fragmenting the PN, or copies of it, to form fragments, (iii) performing PCR amplification and thereby homologously recombining the fragments to form a shuffled pool of recombined PNs, which are not present in the selected library of (i).

28 Claims, 15 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 15

L3: Entry 19 of 48 File: USPT Nov 3, 1998

DOCUMENT-IDENTIFIER: US 5830721 A
TITLE: DNA mutagenesis by random fragmentation and reassembly

DEPR:
One variation involves the use of multiple binding targets (multiple epitope species, multiple receptor species), such that a scFv library can be simultaneously screened for a multiplicity of scFv which have different binding specificities. Given that the size of a scFv library often limits the diversity of potential scFv sequences, it is typically desirable to us scFv libraries of as large a size as possible. The time and economic considerations of generating a number of very large polysome scFv-display libraries can become prohibitive. To avoid this substantial problem, multiple predetermined epitope species (receptor species) can be concomitantly screened in a single library, or sequential screening against a number of epitope species can be used. In one variation, multiple target epitope species, each encoded on a separate bead (or subset of beads), can be mixed and incubated with a polysome-display scFv library under suitable binding conditions. The collection of beads, comprising multiple epitope species, can then be used to isolate, by affinity selection, scFv library members. Generally, subsequent affinity screening rounds can include the same mixture of beads, subsets thereof, or beads containing only one or two individual epitope species. This approach affords efficient screening, and is compatible with laboratory automation, batch processing, and high throughput screening methods.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 20. Document ID: US 5824485 A

L3: Entry 20 of 48 File: USPT Oct 20, 1998

US-PAT-NO: 5824485
DOCUMENT-IDENTIFIER: US 5824485 A

TITLE: Methods for generating and screening novel metabolic pathways

DATE-ISSUED: October 20, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Thompson; Katie A.	Del Mar	CA	N/A	N/A
Foster; Lyndon M.	Carlsbad	CA	N/A	N/A
Peterson; Todd C.	Chula Vista	CA	N/A	N/A
Nasby; Nicole Marie	San Diego	CA	N/A	N/A
Brian; Paul	San Diego	CA	N/A	N/A

US-CL-CURRENT: 435/6; 435/320.1, 435/455, 435/471, 435/489, 435/69.1, 435/91.41, 435/DIG.23, 435/DIG.26, 435/DIG.47, 435/DIG.5, 435/DIG.6, 435/DIG.7, 435/DIG.8, 536/23.1

ABSTRACT:

The present invention relates to a novel drug discovery system for generating and screening molecular diversity. The system provides methods for mixing and cloning genetic materials from a plurality of species of organisms in combinatorial gene expression libraries to generate novel metabolic pathways and classes of compounds. The system also involves methods for pre-screening or identifying for host organisms containing a library that are capable of generating such novel pathways and compounds. The host organisms may be useful in drug screening for particular diseases, and in commercial production of compounds of interest. The methods of the invention are also useful in preserving the genomes of organisms that are known or prospective sources of drugs.

45 Claims, 25 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 21

L3: Entry 20 of 48 File: USPT Oct 20, 1998

DOCUMENT-IDENTIFIER: US 5824485 A
TITLE: Methods for generating and screening novel metabolic pathways

ABPL:
The present invention relates to a novel drug discovery system for generating and screening molecular diversity. The system provides methods for mixing and cloning genetic materials from a plurality of species of organisms in combinatorial gene expression libraries to generate novel metabolic pathways and classes of compounds. The system also involves methods for pre-screening or identifying for host organisms containing a library that are capable of generating such novel pathways and compounds. The host organisms may be useful in drug screening for particular diseases, and in commercial production of compounds of interest. The methods of the invention are also useful in preserving the genomes of organisms that are known or prospective sources of drugs.

BSPR:
In another embodiment, the invention involves the construction of combinatorial chimeric pathway expression libraries in which genetic material derived from one or more species of donor organism is randomly combined, cloned, and expressed in the host organism. Such libraries generate random combinations of genes from multiple pathways and organisms, which gives rise to metabolic pathways and discrete gene sets previously non-existent in nature. The term "discrete gene set" refers to any assemblage of two or more genes obtained from the ligation of genes from one or more pathway or organism in a combinatorial gene expression library. The plurality of gene products are capable of functioning in the host organism, where they interact to form novel chimeric metabolic pathways that produce novel classes of compounds. Thus, the diversity of molecular structures available for drug screening is increased by mixing the genetic material of the

extant pathways and organisms in the combinatorial chimeric gene expression library.

BSPR:
A "combinatorial natural pathway expression library" is a library of expression constructs prepared from genetic material derived from a plurality of species of donor organisms, in which genes present in the genetic material are operably associated with regulatory regions that drive expression of the genes in an appropriate host organism. The combinatorial expression library utilizes host organisms that are capable of producing functional gene products of the donor organisms. The genetic material in each of the host organism encodes naturally-occurring biochemical pathways or portions thereof from one of the donor organisms.

DEPR:
More particularly, the invention provides methods for constructing and screening combinatorial gene expression libraries. These libraries comprise random assortments of gene products of multiple species which are in some cases allowed to interact with each other in the expression host, and result in some cases in the formation of novel biochemical pathways and/or the production of novel classes of compounds. Moreover, the libraries of the invention provide efficient access to otherwise inaccessible sources of molecular diversity.

DEPR:
A "combinatorial chimeric pathway expression library" is a library of expression constructs prepared from randomly concatenated genetic material derived from a plurality of species of donor organisms, in which genes present in the genetic material are operably associated with regulatory regions that drives expression of the genes in an appropriate host organism. The host organisms used are capable of producing functional gene products of the donor organisms. Upon expression in the host organism, gene products of the donor organism(s) may interact to form novel chimeric biochemical pathways.

DEPR:
In another embodiment of the invention, a combinatorial chimeric pathway gene expression library can be constructed in which the genetic materials from one or multiple donor organisms are randomly concatenated prior to introduction into the host organism. Thus, each host organism in the library may individually contain a unique, random combination of genes derived from the various donor pathways or organisms. FIG. 2 shows the arrangement of genes and regulatory regions in an expression construct of a combinatorial chimeric pathway gene expression library. For the most part, such combinations of genes in the library do not occur in nature. Upon expression, the functional gene products of the various donor pathways or organisms interact with each other in individual host organisms to generate combinations of biochemical reactions which result in novel chimeric metabolic pathways and/or production of novel compounds. Collectively, the genetic resources of the donor organisms in the library are translated into a diversity of chemical compounds that may not be found in individual donor organisms.

DEPR:
The present invention relates to the construction and uses of combinatorial gene expression libraries, wherein the host organisms contain genetic material encoding natural biochemical pathways or portions thereof that is derived from a plurality of species of donor organisms, and are capable of producing functional gene products of the donor organisms. Biochemical pathways or portions thereof of the donor organisms are thus functionally reconstituted in individual host organisms of a library. Novel activities and compounds of such biochemical pathways may be more accessible to screening by traditional drug discovery techniques or by methods provided herein.

DEPR:
While not limited to any theory of how novel pathways or compounds are generated in a combinatorial chimeric pathway gene expression library, the coexpression of functional heterologous genes derived from one or a plurality of species of donor organisms enables the gene products to interact in vivo with each other, and with elements of the host organism. Through such interactions, new sets of biochemical reactions will arise, some of which can act in concert to form a chimeric biochemical pathway. The heterologous gene products may encounter substrates,

cofactors and signalling molecules that are not present in their respective donor organism. Such substrates, cofactors and signalling molecules may be supplied by the host organism, by other heterologous gene products that are coexpressing in the same host organism, or from the medium.

DEPR:
The combinatorial chimeric pathway expression libraries of the invention may be assembled according to the principles described in section 5.1.3. In order to allow the random concatenation of DNA fragments from multiple species of donor organisms, the procedure for library assembly may be modified by including the following steps: generation of smaller genomic DNA fragments, ligation with regulatory sequences such as promoters and terminators to form gene cassettes, and concatenation of the gene cassettes.

CLPR:
1. A combinatorial gene expression library, comprising a pool of expression constructs, each expression construct containing one or more cDNA or genomic DNA fragments, wherein the cDNA or genomic DNA fragments in the pool of expression constructs are derived from a plurality of species of donor organisms, and wherein the cDNA or genomic DNA fragments in each expression construct are operably-associated each with one or more regulatory regions that drives expression of genes encoded by the cDNA or genomic DNA fragments in an appropriate host organism.

CLPR:
3. A biased combinatorial gene expression library, comprising a pool of expression constructs, each expression construct containing cDNA or genomic DNA fragments preselected from a plurality of species of donor organisms for a specific property, in which the cDNA or genomic DNA fragments are operably-associated with one or more regulatory regions that drive expression of genes encoded by the cDNA or genomic DNA fragments in an appropriate host organism.

CLPR:
19. A method for making a combinatorial gene expression library, comprising ligating a DNA vector to one or more cDNA or genomic DNA fragments to generate a library of expression constructs, wherein the cDNA or genomic DNA fragments in the library of expression constructs are obtained from a plurality of species of donor organisms, and wherein genes contained in the cDNA or genomic DNA fragments are operably-associated with their native or exogenous regulatory regions which drive expression of the genes in an appropriate host cell.

CLPR:
21. A method for making a biased combinatorial gene expression library, comprising ligating a DNA vector to one or more cDNA or genomic DNA fragments to generate a library of expression constructs, wherein the cDNA or genomic DNA fragments are obtained from a plurality of species of donor organisms and are selected for a specific property, and wherein genes contained in the cDNA or genomic DNA fragments are operably-associated with their native or exogenous regulatory regions which drive expression of the genes in an appropriate host cell.

☐ 21. Document ID: US 5811238 A

L3: Entry 21 of 48 File: USPT Sep 22, 1998

US-PAT-NO: 5811238
DOCUMENT-IDENTIFIER: US 5811238 A

TITLE: Methods for generating polynucleotides having desired characteristics by iterative selection and recombination

DATE-ISSUED: September 22, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Stemmer; Willem P. C.	Los Gatos	CA	N/A	N/A
Crameri; Andreas	Mountain View	CA	N/A	N/A

US-CL-CURRENT: 435/6; 435/440, 435/91.2, 435/91.5

ABSTRACT:

A method for DNA reassembly after random fragmentation, and its application to mutagenesis of nucleic acid sequences by in vitro or in vivo recombination is described. In particular, a method for the production of nucleic acid fragments or polynucleotides encoding mutant proteins is described. The present invention also relates to a method of repeated cycles of mutagenesis, shuffling and selection which allow for the directed molecular evolution in vitro or in vivo of proteins.

22 Claims, 22 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 22

L3: Entry 21 of 48 File: USPT Sep 22, 1998

DOCUMENT-IDENTIFIER: US 5811238 A
TITLE: Methods for generating polynucleotides having desired characteristics by iterative selection and recombination

DEPR:
One variation involves the use of multiple binding targets (multiple epitope species, multiple receptor species), such that a scFv library can be simultaneously screened for a multiplicity of scFv which have different binding specificities. Given that the size of a scFv library often limits the diversity of potential scFv sequences, it is typically desirable to us scFv libraries of as large a size as possible. The time and economic considerations of generating a number of very large polysome scFv-display libraries can become prohibitive. To avoid this substantial problem, multiple predetermined epitope species (receptor species) can be concomitantly screened in a single library, or sequential screening against a number of epitope species can be used. In one variation, multiple target epitope species, each encoded on a separate bead (or subset of beads), can be mixed and incubated with a polysome-display scFv library under suitable binding conditions. The collection of beads, comprising multiple epitope species, can then be used to isolate, by affinity selection, scFv library members. Generally, subsequent affinity screening rounds can include the same mixture of beads, subsets thereof, or beads containing only one or two individual epitope species. This approach affords efficient screening, and is compatible with laboratory automation, batch processing, and high throughput screening methods.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 22. Document ID: US 5783431 A

L3: Entry 22 of 48 File: USPT Jul 21, 1998

US-PAT-NO: 5783431
DOCUMENT-IDENTIFIER: US 5783431 A

TITLE: Methods for generating and screening novel metabolic pathways

DATE-ISSUED: July 21, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Peterson; Todd C.	Chula Vista	CA	N/A	N/A
Foster; Lyndon M.	Carlsbad	CA	N/A	N/A
Brian; Paul	San Diego	CA	N/A	N/A

US-CL-CURRENT: 435/455; 435/320.1, 435/463, 435/466, 435/471, 435/472, 435/474, 435/489, 536/23.1

ABSTRACT:

The present invention relates to a novel drug discovery system for generating and screening molecular diversity. The system provides methods for mixing and cloning genetic materials from a plurality of species of organisms in combinatorial gene expression libraries to generate novel metabolic pathways and classes of compounds. The system also provides mobilizable combinatorial gene expression libraries that can be transferred from one species of host organism to another for expression. Also provided are specialized cloning vectors for making mobilizable gene expression libraries. The system also involves methods for pre-screening or identifying for host organisms containing a library that are capable of generating such novel pathways and compounds.

25 Claims, 27 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 23

L3: Entry 22 of 48 File: USPT Jul 21, 1998

DOCUMENT-IDENTIFIER: US 5783431 A
TITLE: Methods for generating and screening novel metabolic pathways

ABPL:
The present invention relates to a novel drug discovery system for generating and screening molecular diversity. The system provides methods for mixing and cloning genetic materials from a plurality of species of organisms in combinatorial gene expression libraries to generate novel metabolic pathways and classes of compounds. The system also provides mobilizable combinatorial gene expression libraries that can be transferred from one species of host organism to another for expression. Also provided are specialized cloning vectors for making mobilizable gene expression libraries. The system also involves methods for pre-screening or identifying for host organisms containing a library that are capable of generating such novel pathways and compounds.

BSPR:
In another embodiment, the invention involves the construction of combinatorial chimeric pathway expression libraries in which genetic material derived from one or more species of donor organism is randomly combined, cloned, and expressed in the host organism. Such libraries generate random combinations of genes from multiple pathways and organisms, which gives rise to metabolic pathways and discrete gene sets previously non-existent in nature. The term "discrete gene set" refers to any assemblage of two or more genes obtained from the ligation of genes from one or more pathway or organism in a combinatorial gene expression library. The plurality of gene products are capable of functioning in the host organism, where they interact to form novel chimeric metabolic pathways that produce novel classes of compounds. Thus, the diversity of molecular structures available for drug screening is increased by mixing the genetic material of the extant pathways and organisms in the combinatorial chimeric gene expression library.

BSPR:

A "combinatorial natural pathway expression library" is a library of expression constructs prepared from genetic material derived from a plurality of species of donor organisms, in which genes present in the genetic material are operably associated with regulatory regions that drive expression of the genes in an appropriate host organism. The combinatorial expression library utilizes host organisms that are capable of producing functional gene products of the donor organisms. The genetic material in each of the host organism encodes naturally-occurring biochemical pathways or portions thereof from one of the donor organisms.

DEPR:
More particularly, the invention provides methods for constructing and screening combinatorial gene expression libraries. These libraries comprise random assortments of gene products of multiple species which are in some cases allowed to interact with each other in the expression host, and result in some cases in the formation of novel biochemical pathways and/or the production of novel classes of compounds. Moreover, the libraries of the invention provide efficient access to otherwise inaccessible sources of molecular diversity. Some of the libraries of the invention can be transferred from one species of host organism to another species or strain of host organism.

DEPR:
A "combinatorial chimeric pathway expression library" is a library of expression constructs prepared from randomly concatenated genetic material derived from a plurality of species of donor organisms, in which genes present in the genetic material are operably associated with regulatory regions that drives expression of the genes in an appropriate host organism. The host organisms used are capable of producing functional gene products of the donor organisms. Upon expression in the host organism, gene products of the donor organism(s) may interact to form novel chimeric biochemical pathways.

DEPR:
In another embodiment of the invention, a combinatorial chimeric pathway gene expression library can be constructed in which the genetic materials from one or multiple donor organisms are randomly concatenated prior to introduction into the host organism. Thus, each host organism in the library may individually contain a unique, random combination of genes derived from the various donor pathways or organisms. FIG. 2 shows the arrangement of genes and regulatory regions in an expression construct of a combinatorial chimeric pathway gene expression library. For the most part, such combinations of genes in the library do not occur in nature. Upon expression, the functional gene products of the various donor pathways or organisms interact with each other in individual host organisms to generate combinations of biochemical reactions which result in novel chimeric metabolic pathways and/or production of novel compounds. Collectively, the genetic resources of the donor organisms in the library are translated into a diversity of chemical compounds that may not be found in individual donor organisms.

DEPR:
By using a shuttle vector with the appropriate replication origins, transfer origin(s) and selection mechanisms to construct a library, the DNA sequences of the donor organisms in a library may readily be mobilized from one initial species of host organism to a variety of alternative species of host organisms where the donor DNA sequences can be stably maintained, replicated and expressed. Thus, mobilizable gene expression libraries that are constructed with a shuttle vector, and that can be mobilized into multiple host organisms by conjugation are within the scope of the invention.

DEPR:
The present invention relates to the construction and uses of combinatorial gene expression libraries, wherein the host organisms contain genetic material encoding natural biochemical pathways or portions thereof that is derived from a plurality of species of donor organisms, and are capable of producing functional gene products of the donor organisms. Biochemical pathways or portions thereof of the donor organisms are thus functionally reconstituted in individual host organisms of a library. Novel activities and compounds of such biochemical pathways may be more accessible to screening by traditional drug discovery techniques or by methods provided herein.

DEPR:
While not limited to any theory of how novel pathways or compounds are generated in a combinatorial chimeric pathway gene expression library, the coexpression of functional heterologous genes derived from one or a plurality of species of donor organisms enables the gene products to interact in vivo with each other, and with elements of the host organism. Through such interactions, new sets of biochemical reactions will arise, some of which can act in concert to form a chimeric biochemical pathway. The heterologous gene products may encounter substrates, cofactors and signalling molecules that are not present in their respective donor organism. Such substrates, cofactors and signalling molecules may be supplied by the host organism, by other heterologous gene products that are coexpressing in the same host organism, or from the medium.

DEPR:
The combinatorial chimeric pathway expression libraries of the invention may be assembled according to the principles described in section 5.1.3. In order to allow the random concatenation of DNA fragments from multiple species of donor organisms, the procedure for library assembly may be modified by including the following steps: generation of smaller genomic DNA fragments, ligation with regulatory sequences such as promoters and terminators to form gene cassettes, and concatenation of the gene cassettes.

CLPR:
1. A mobilizable combinatorial gene expression library, comprising a pool of expression constructs, each expression construct comprising a shuttle vector that replicates in different species or strains of host cell, said shuttle vector containing one or more cDNA or genomic DNA fragments, wherein the cDNA or genomic DNA fragments in the pool of expression constructs are derived from a plurality of species of donor organisms, and wherein the cDNA or genomic DNA fragments are each operably-associated with one or more regulatory regions that drives expression of genes encoded by the cDNA or genomic DNA fragments in an appropriate host organism.

CLPR:
13. A method for making a mobilizable combinatorial gene expression library, comprising ligating a shuttle vector that replicates in different species or strains of host cell, to one or more cDNA or genomic DNA fragments to form a pool of expression constructs, wherein said cDNA or genomic DNA fragments in the pool of expression constructs are obtained from a plurality of species of donor organisms, and wherein the genes contained in the cDNA or genomic DNA fragments are each operably-associated with their native or exogenous regulatory regions which drive expression of the genes in an appropriate host cell.

CLPR:
18. A method for making a combinatorial gene expression library comprising transferring a pool of expression constructs in a species of host organism to another species or strain of host organism, said expression construct comprising a shuttle vector that replicates in different species or strains of host cell, said shuttle vector comprising one or more cDNA or genomic DNA fragments, wherein the cDNA or genomic DNA fragments in the pool of expression constructs are obtained from a plurality of species of donor organisms, and wherein the genes contained in the cDNA or genomic DNA fragments are each operably-associated with their native or exogenous regulatory regions which drive expression of the genes in an appropriate host cell.

CLPR:
21. A method for making a biased combinatorial gene expression library, comprising ligating a DNA vector to one or more cDNA or genomic DNA fragments to generate a library of expression constructs, wherein the cDNA or genomic DNA fragments in the library are obtained from a plurality of species of donor organisms and are selected for a specific property, and wherein genes contained in the cDNA or genomic DNA fragments are each operably-associated with their native or exogenous regulatory regions which drive expression of the genes in an appropriate host cell.

☐ 23. Document ID: US 5773213 A

L3: Entry 23 of 48 File: USPT Jun 30, 1998

US-PAT-NO: 5773213
DOCUMENT-IDENTIFIER: US 5773213 A

TITLE: Method for conducting sequential nucleic acid hybridization steps

DATE-ISSUED: June 30, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gullans; Steven R.	Natick	MA	N/A	N/A
Kojima; Ryoji	Boston	MA	N/A	N/A
Randall; Jeffrey	Acton	MA	N/A	N/A

US-CL-CURRENT: 435/6; 435/91.1, 435/91.2, 536/24.32, 536/24.33

ABSTRACT:

A method for conducting sequential nucleic acid hybridization steps is described, whereby the ability of earlier-used primers or probes to participate in subsequent hybridization steps can be minimized, even though the differences between primer lengths are relatively small. It also relates to a rapid and quantitative method for the sequential synthesis of polynucleotide sequences by using a plurality of oligonucleotide primers, with the earlier utilized primers causing a minimum of interference with the subsequent primed synthesis reactions, yet without the need for intermediate purification steps. One preferred embodiment described is a method for differential display reverse-transcription polymerase chain reaction (DDRT-PCR), wherein complementary DNAs (cDNAs) are first synthesized using oligo-dT-primed reverse transcription (RT), and selected subsets of said cDNAs are then amplified using a second primer in a polymerase chain reaction (PCR), with a minimum degree of background being caused in the PCR step by residual amounts of the oligo-dT primer.

17 Claims, 9 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 9

L3: Entry 23 of 48 File: USPT Jun 30, 1998

DOCUMENT-IDENTIFIER: US 5773213 A
TITLE: Method for conducting sequential nucleic acid hybridization steps

BSPR:
The secondary use of the reverse transcription primer as the intended primer for the PCR reaction eliminated the possibility of such a background problem. This method has enabled researchers to identify and characterize several tumor suppressor genes [4, 8]. However, the PCR-amplified strands that result from this method all begin at the 5' end of the poly-A.sup.+ tail, and extended a maximum of 600 base pairs in the 5' direction. This region is typically polymorphic, often contains repetitive sequences, and, because it generally contains a non-coding region, offers no information regarding the potential function of differentially expressed genes. In addition, because the products are typically short fragments (<600 bp) that can contain repetitive sequences, they often hybridize to multiple mRNA species in a northern blot or to multiple clones in a cDNA library. Although significant methodological improvements have been offered [1, 2], the Liang and Pardee method still has the significant drawback that it preferentially amplifies the non-coding 3' untranslated region (3' UTR) of cDNAs during PCR.

☐ 24. Document ID: US 5770356 A

L3: Entry 24 of 48 File: USPT Jun 23, 1998

US-PAT-NO: 5770356
DOCUMENT-IDENTIFIER: US 5770356 A

TITLE: Phagemids coexpressing a surface receptor and a surface heterologous protein

DATE-ISSUED: June 23, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Light, II; James Paul	San Diego	CA	N/A	N/A
Lerner; Richard A.	La Jolla	CA	N/A	N/A

US-CL-CURRENT: 435/5; 435/252.33, 435/320.1, 435/475, 435/6, 435/7.1

ABSTRACT:

A filamentous phage is described comprising a matrix that includes a heterologous polypeptide fused to a first filamentous phage coat protein membrane anchor and a heterodimeric receptor comprised of first and second receptor polypeptides, wherein one of the receptor polypeptides is fused to a second filamentous phage coat protein membrane anchor. Filamentous phage expressing anchored heterodimeric receptors and dimers of heterologous polypeptides where a first subunit of the dimer is fused to a coat protein membrane anchor and the second subunit of the dimer is soluble heteromeric receptor are also described.

45 Claims, 19 Drawing figures Exemplary Claim Number: 26
Number of Drawing Sheets: 13

L3: Entry 24 of 48 File: USPT Jun 23, 1998

DOCUMENT-IDENTIFIER: US 5770356 A
TITLE: Phagemids coexpressing a surface receptor and a surface heterologous protein

DEPR:
The use of the above particle segregation methods provides a means for screening a population of filamentous phage particles present in a phage library of this invention. As applied to a phage library, screening can be utilized to enrich the library for one or more particles that express a heterodimer having a preselected ligand binding specificity. Where the library is designed to contain multiple species of heterodimers that all have some detectable measure of ligand binding activity, but differ in protein structure, antigenicity, ligand binding affinity or avidity, and the like, the screening methods can be utilized sequentially to first produce a library enriched for a preselected binding specificity, and then to produce a second library further enriched by further screening comprising one or more isolated phage particles. Methods for measuring ligand binding activities, antigenicity and the like interactions between a ligand and a receptor are generally well known and are not discussed further as they are not essential features of the present invention.

DEPR:
In the method, an rDNA vector that expresses the heterologous fusion polypeptide is combined with the provided rDNA vector (in one of its various forms) within a single E. coli host cell such that the host cell contains both the rDNA vector for expressing the heterologous fusion polypeptide and the rDNA vector for expressing the heterodimeric receptor. The combination can be repeated multiple times with multiple members of the library, such as in a batch process in which multiple species are present. Thus, a heterologous fusion polypeptide-expressing rDNA vector is combined with a pre-existing library of rDNA vectors that can express a heterodimeric receptor, thereby forming the phage library of this invention.

☐ 25. Document ID: US 5759817 A

L3: Entry 25 of 48 File: USPT Jun 2, 1998

US-PAT-NO: 5759817
DOCUMENT-IDENTIFIER: US 5759817 A

TITLE: Heterodimeric receptor libraries using phagemids

DATE-ISSUED: June 2, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Barbas; Carlos	San Diego	CA	N/A	N/A

US-CL-CURRENT: 435/69.7; 435/320.1, 435/7.1, 435/DIG.47, 530/387.1, 530/387.3

ABSTRACT:

Filamentous phage comprising a matrix of cpVIII proteins encapsulating a genome encoding first and second polypeptides of an antogenously assembling receptor, such as an antibody, and a receptor comprised of the first and second polypeptides surface-integrated into the matrix via a cpVIII membrane anchor domain fused to at least one of the polypeptides with a mutagenized CDR3 region.

26 Claims, 17 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 12

L3: Entry 25 of 48 File: USPT Jun 2, 1998

DOCUMENT-IDENTIFIER: US 5759817 A
TITLE: Heterodimeric receptor libraries using phagemids

DEPR:
The use of the above particle segregation methods provides a means for screening a population of filamentous phage particles present in a phage library of this invention. As applied to a phage library, screening can be utilized to enrich the library for one or more particles that express a heterodimer having a preselected ligand binding specificity. Where the library is designed to contain multiple species of heterodimers that all have some detectable measure of ligand binding activity, but differ in protein structure, antigenicity, ligand binding affinity or avidity, and the like, the screening methods can be utilized sequentially to first produce a library enriched for a preselected binding specificity, and then to produce a second library further enriched by further screening comprising one or more isolated phage particles. Methods for measuring ligand binding activities, antigenicity and the like interactions between a ligand and a receptor are generally well known and are not discussed further as they are not essential features of the present invention.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 26. Document ID: US 5723598 A

L3: Entry 26 of 48 File: USPT Mar 3, 1998

US-PAT-NO: 5723598
DOCUMENT-IDENTIFIER: US 5723598 A

TITLE: Encoded combinatorial chemical libraries

DATE-ISSUED: March 3, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lerner; Richard	La Jolla	CA	N/A	N/A
Janda; Kim	San Diego	CA	N/A	N/A
Brenner; Sydney	Cambridge	N/A	N/A	GB2

US-CL-CURRENT: 536/25.3; 530/335, 530/336, 530/337

ABSTRACT:

The present invention describes an encoded combinatorial chemical library comprised of a plurality of bifunctional molecules having both a chemical polymer and an identifier oligonucleotide sequence that defines the structure of the chemical polymer. Also described are the bifunctional molecules of the library, and methods of using the library to identify chemical structures within the library that bind to biologically active molecules in preselected binding interactions.

5 Claims, 2 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 2

L3: Entry 26 of 48 File: USPT Mar 3, 1998

DOCUMENT-IDENTIFIER: US 5723598 A
TITLE: Encoded combinatorial chemical libraries

BSPR:
In another embodiment, the invention contemplates a library comprising a plurality of species of bifunctional molecules, thereby forming a repertoire of chemical diversity.

DEPR:
An encoded combinatorial chemical library is a composition comprising a plurality of species of bifunctional molecules that each define a different chemical structure and that each contain a unique identifier oligonucleotide whose nucleotide sequence defines the corresponding chemical structure.

DEPR:
A library of this invention is a repertoire of chemical diversity comprising a plurality of species of bifunctional molecules according to the present invention. The plurality of species in a library defines a family of chemical diversity whose species each have a different chemical moiety. Thus the library can define a family of peptides, lipids, oligosaccarides or any of the other classes of chemical polymers recited previously.

DEPR:
The number of different species in a library represents the complexity of a library and is defined by the polymer length of the chemical moiety, and by the size of the chemical unit alphabet that can be used to build the chemical unit polymer. The number of different species referred to by the phrase "plurality of species" in a library can be defined by the formula V.sup.a, i.e., V to power of a (exponent a). V represents the alphabet size, i.e., the number of different chemical units X available for use in the chemical moiety. "a" is an exponent to V and represents the number of chemical units of X forming the polymer A, i.e., the length of polymer A.

☐ 27. Document ID: US 5695932 A

L3: Entry 27 of 48 File: USPT Dec 9, 1997

US-PAT-NO: 5695932
DOCUMENT-IDENTIFIER: US 5695932 A

TITLE: Telomerase activity assays for diagnosing pathogenic infections

DATE-ISSUED: December 9, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
West; Michael D.	Belmont	CA	N/A	N/A
Shay; Jerry	Dallas	TX	N/A	N/A
Wright; Woodring	Arlington	TX	N/A	N/A
Blackburn; Elizabeth H.	San Francisco	CA	N/A	N/A
McEachern; Michael J.	San Francisco	CA	N/A	N/A

US-CL-CURRENT: 435/6; 435/91.1

ABSTRACT:

Method and compositions are provided for the determination of telomere length and telomerase activity, as well as the ability to inhibit telomerase activity in the treatment of proliferative diseases. Particularly, primers are elongated under conditions which minimize interference from other genomic sequences, so as to obtain accurate determinations of telomeric length or telomerase activity. In addition, compositions are provided for intracellular inhibition of telomerase activity and means are shown for slowing the loss of telomeric repeats in aging cells.

8 Claims, 44 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 32

L3: Entry 27 of 48 File: USPT Dec 9, 1997

DOCUMENT-IDENTIFIER: US 5695932 A
TITLE: Telomerase activity assays for diagnosing pathogenic infections

DRPR:
FIG. 30 shows sequences of telomeric repeats from several budding yeast species. Specifically, telomere-enriched libraries were constructed from genomic DNA by standard methods. Uncut yeast genomic DNA was ligated to a blunt-ended linearized plasmid vector and then this ligated mix was digested with a restriction enzyme that cleaves both within the vector's polylinker and within a few kilobases of at least some of the putative telomeric ends of the species in question. No enzymatic pre-treatment was done to produce blunt-ends of the telomeres in the genomic DNA prior to the initial ligations. Plasmids were then recircularized with T4DNA ligase, and transformed into E. coli cells prior to screening for putative telomere clones by colony hybridization. The libraries from C. maltosa, C. pseudotropicalis, two strains of C. tropicalis, and K. lactis ATCC 32143, species which showed multiple bands that cross hybridized to the C. albicans telomeric repeat probe, were screened with this probe. A cloned S. cerevisiae telomere probe (repeat unit TG.sub.2-3 (GT).sub.1-3,) was used to screen the telomere--enriched library from C. glabrata, whose genomic DNA cross--hybridized with this, but not with the C. albicans telomeric repeat probe. C. guillermondii DNA did not appreciably cross-hybridize with either the C. albicans or the S. cerevisiae telomeric probes at the stringencies tested. The telomere--enriched library from this species was screened using total genomic C. guillermondii DNA as a probe. This procedure can be used to identify all clones containing repetitive sequences and we reasoned that telomeres should be a reasonable percentage of the repetitive sequences found in telomere enriched libraries. Typically, a few hundred E. coli transformants were obtained for each small library and up to nine putative telomere clones were obtained from each. Nine repetitive DNA clones were obtained from C. guillermondii, three of which proved to be telomeric.

☐ 28. Document ID: US 5691136 A

L3: Entry 28 of 48 File: USPT Nov 25, 1997

US-PAT-NO: 5691136
DOCUMENT-IDENTIFIER: US 5691136 A

TITLE: Fingerprinting bacterial strains using repetitive DNA sequence amplification

DATE-ISSUED: November 25, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lupski; James R.	Houston	TX	N/A	N/A
Versalovic; James	Houston	TX	N/A	N/A
Koeuth; Thearith	Houston	TX	N/A	N/A

US-CL-CURRENT: 435/6; 435/91.2

ABSTRACT:

Oligonucleotide primers and methods for identifying strains of bacteria by genomic fingerprinting are described. The methods are applicable to a variety of samples. The testing procedure includes amplifying the bacterial DNA in the sample to be tested by adding a pair of outwardly-directed primers to the sample. The primers are capable of hybridizing to repetitive DNA sequences in the bacterial DNA and extending outwardly from one hybridizable repetitive sequence to another hybridizable repetitive sequence. After amplification the extension products are separated by size and the specific strain of bacteria is determined by measuring the pattern of sized extension products. The procedure to identify strains of bacteria by fingerprinting has a variety of uses including: identifying bacteria in infections, agriculture and horticulture plots, bioremediation, food monitoring, production monitoring and quality assurance and quality control.

113 Claims, 19 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 19

L3: Entry 28 of 48 File: USPT Nov 25, 1997

DOCUMENT-IDENTIFIER: US 5691136 A
TITLE: Fingerprinting bacterial strains using repetitive DNA sequence amplification

CLPR:
12. The method of claim 1, wherein the sample contains a plurality of species of bacteria and wherein each specific species of bacteria is distinguished by comparing the size pattern of extension products to a library of known fingerprints to determine the identity of each specific species of bacteria in the sample.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 29. Document ID: US 5688696 A

L3: Entry 29 of 48 File: USPT Nov 18, 1997

US-PAT-NO: 5688696
DOCUMENT-IDENTIFIER: US 5688696 A

TITLE: Combinatorial libraries having a predetermined frequency of each species of test compound

DATE-ISSUED: November 18, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lebl; Michal	Oro Valley	AZ	N/A	N/A

US-CL-CURRENT: 436/518; 435/6, 435/7.1, 436/501, 436/528, 436/529, 436/530, 436/531, 436/543, 530/333, 530/334

ABSTRACT:

A technique for generating nonrandom combinatorial libraries on solid phase supports in which each of a set of predetermined species of test compounds is present on a predetermined number of solid phase supports, preferably on only one, and each solid phase support has only a single species of test compound. Each of the predetermined species of test compounds is prepared with absolute certainty because the technique does not employ any random division of the solid phase supports. Rather, the method is based on the stepwise division of a continuous solid phase support matrix prior to each synthetic step in which more than one type of subunit is added. Non-limiting examples of matrices of the solid phase supports include polypropylene membranes, polytetrafluoropropylene membranes and cotton thread. The combinatorial libraries made by the technique are also disclosed.

30 Claims, 3 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 3

L3: Entry 29 of 48 File: USPT Nov 18, 1997

DOCUMENT-IDENTIFIER: US 5688696 A
TITLE: Combinatorial libraries having a predetermined frequency of each species of test compound

BSPR:
The present invention concerns the field of combinatorial libraries of species of test compound that are synthesized on solid phase supports. A combinatorial library is a collection of multiple species of chemical compounds that consist of randomly selected subunits. Such libraries are useful because they can be screened to identify a ligand for an acceptor of interest. More particularly the invention concerns methods for constructing such libraries when the solid phase support is a material that can be readily fashioned into further divisible pieces.

☐ 30. Document ID: US 5658727 A

L3: Entry 30 of 48 File: USPT Aug 19, 1997

US-PAT-NO: 5658727
DOCUMENT-IDENTIFIER: US 5658727 A

TITLE: Heterodimeric receptor libraries using phagemids

DATE-ISSUED: August 19, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Barbas; Carlos	La Jolla	CA	N/A	N/A
Kang; Angray	Carlsbad	CA	N/A	N/A
Lerner; Richard A.	La Jolla	CA	N/A	N/A

US-CL-CURRENT: 435/6; 435/235.1, 435/320.1, 435/91.2, 530/387.3

ABSTRACT:

Filamentous phage comprising a matrix of cpVIII proteins encapsulating a genome encoding first and second polypeptides of an antogenously assembling receptor, such as an antibody, and a receptor comprised of the first and second polypeptides surface-integrated into the matrix via a filamentous phage coat protein membrane anchor domain fused to at least one of the polypeptides.

36 Claims, 19 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 14

L3: Entry 30 of 48 File: USPT Aug 19, 1997

DOCUMENT-IDENTIFIER: US 5658727 A
TITLE: Heterodimeric receptor libraries using phagemids

DEPR:
The use of the above particle segregation methods provides a means for screening a population of filamentous phage particles present in a phage library of this invention. As applied to a phage library, screening can be utilized to enrich the library for one or more particles that express a heterodimer having a preselected ligand binding specificity. Where the library is designed to contain multiple species of heterodimers that all have some detectable measure of ligand binding activity, but differ in protein structure, antigenicity, ligand binding affinity or avidity, and the like, the screening methods can be utilized sequentially to first produce a library enriched for a preselected binding specificity, and then to produce a second library further enriched by further screening comprising one or more isolated phage particles. Methods for measuring ligand binding activities, antigenicity and the like interactions between a ligand and a receptor are generally well known and are not discussed further as they are not essential features of the present invention.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 31. Document ID: US 5645986 A

L3: Entry 31 of 48 File: USPT Jul 8, 1997

US-PAT-NO: 5645986
DOCUMENT-IDENTIFIER: US 5645986 A

TITLE: Therapy and diagnosis of conditions related to telomere length and/or telomerase activity

DATE-ISSUED: July 8, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
West; Michael D.	San Carlos	CA	N/A	N/A
Harley; Calvin B.	Palo Alto	CA	N/A	N/A
Strahl; Catherine M.	San Francisco	CA	N/A	N/A
McEachern; Michael J.	San Francisco	CA	N/A	N/A
Shay; Jerry	Dallas	TX	N/A	N/A
Wright; Woodring E.	Arlington	TX	N/A	N/A
Blackburn; Elizabeth H.	San Francisco	CA	N/A	N/A
Vaziri; Homayoun	Toronto	N/A	N/A	CAX

US-CL-CURRENT: 435/6; 435/183, 435/184, 435/194, 435/91.2, 436/63, 536/24.31, 536/24.33

ABSTRACT:

Method and compositions are provided for the determination of telomere length and telomerase activity, as well as the ability to increase or decrease telomerase activity in the treatment of proliferative diseases. Particularly, primers are elongated under conditions which minimize interference from other genomic sequences, so as to obtain accurate determinations of telomeric length or telomerase activity. In addition, compositions are provided for intracellular inhibition of telomerase activity and means are shown for slowing or reversing the loss of telomeric repeats in aging cells.

27 Claims, 55 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 43

L3: Entry 31 of 48 File: USPT Jul 8, 1997

DOCUMENT-IDENTIFIER: US 5645986 A
TITLE: Therapy and diagnosis of conditions related to telomere length and/or telomerase activity

DRPR:
FIG. 30 shows sequences of telomeric repeats from several budding yeast species. Specifically, telomere-enriched libraries were constructed from genomic DNA by standard methods. Uncut yeast genomic DNA was ligated to a blunt-ended linearized plasmid vector and then this ligated mix was digested with a restriction enzyme that cleaves both within the vector's polylinker and within a few kilobases of at least some of the putative telomeric ends of the species in question. No enzymatic pre-treatment was done to produce blunt-ends of the telomeres in the genomic DNA prior to the initial ligations. Plasmids were then recircularized with T4DNA ligase, and transformed into E. coli cells prior to screening for putative telomere clones by colony hybridization. The libraries from C. maltosa, C. pseudotropicalis, two strains of C. tropicalis, and K. lactis ATCC 32143, species which showed multiple bands that cross hybridized to the C. albicans telomeric repeat probe, were screened with this probe. A cloned S. cerevisiae telomere probe (repeat unit TG.sub.2-3 (GT).sub.1-3,) was used to screen the telomere-enriched library from C. glabrata, whose genomic DNA cross-hybridized with this, but not with the C. albicans telomeric repeat probe. C. guillermondii DNA did not appreciably cross-hybridize with either the C. albicans or the S. cerevisiae telomeric probes at the stringencies tested. The telomere-enriched library from this species was screened using total genomic C. guillermondii DNA as a probe. This procedure can be used to identify all clones containing repetitive sequences and we reasoned that telomeres should be a reasonable percentage of the repetitive sequences found in telomere enriched libraries. Typically, a few hundred E. coli transformants were obtained for each small library and up to nine putative telomere clones were obtained from each. Nine repetitive DNA clones were obtained from C. guillermondii, three of which proved to be telomeric.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 32. Document ID: US 5640331 A

L3: Entry 32 of 48 File: USPT Jun 17, 1997

US-PAT-NO: 5640331
DOCUMENT-IDENTIFIER: US 5640331 A

TITLE: Method and apparatus for obtaining species concentrations and reaction rates in a turbulent reacting flow

DATE-ISSUED: June 17, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Dahm; Werner J. A.	Ann Arbor	MI	N/A	N/A
Tryggvason; Gretar	Ann Arbor	MI	N/A	N/A

US-CL-CURRENT: 702/22; 23/306, 436/2, 436/34

ABSTRACT:

A method and apparatus for computing molecular diffusion and chemical reaction within a material wherein shape and time evolution values of one or more material surfaces are determined, and a rate of stretch of each material surface is determined as a function of time. The method includes solving a set of ordinary differential equations at a multiplicity of points on the material surface. The ordinary differential equations are reduced from and represent an approximation of a more complex and complete set of governing partial differential equations. One or more conserved scalars are tracked and conserved scalar values and a gradient of the conserved scalars are determined. A rate of change from the gradient of the conserved scalars is also determined. A mass fraction and a reaction rate of each chemical species of the material is correlated as a function of determined conserved scalar values and a determined gradient of the conserved scalars. The method and apparatus of this invention are particularly useful as a general tool for simulating nitrogen oxides output and other flame properties of a wide class of combustion applications.

3 Claims, 50 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 30

L3: Entry 32 of 48 File: USPT Jun 17, 1997

DOCUMENT-IDENTIFIER: US 5640331 A
TITLE: Method and apparatus for obtaining species concentrations and reaction rates in a turbulent reacting flow

CLPV:
predetermining and storing in a flamelet library a plurality of species concentration values and a plurality of reaction rate values;

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 33. Document ID: US 5627024 A

L3: Entry 33 of 48 File: USPT May 6, 1997

US-PAT-NO: 5627024
DOCUMENT-IDENTIFIER: US 5627024 A

TITLE: Lambdoid bacteriophage vectors for expression and display of foreign proteins

DATE-ISSUED: May 6, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Maruyama; Ichiro	San Diego	CA	N/A	N/A
Maruyama; Hiroko	San Diego	CA	N/A	N/A
Brenner; Sydney	Cambridge	N/A	N/A	GB2

US-CL-CURRENT: 435/5; 435/320.1, 435/475, 435/6, 536/23.4

ABSTRACT:

Lambdoid phage comprising a matrix of proteins encapsulating a genome encoding first and second polypeptides of an autogenously assembling receptor and a receptor comprised of the first and second polypeptides surface-integrated into the matrix via a lambdoid phage tail protein matrix anchor domain fused to at least one of the polypeptides.

22 Claims, 3 Drawing figures Exemplary Claim Number: 1,9,19
Number of Drawing Sheets: 3

L3: Entry 33 of 48 File: USPT May 6, 1997

DOCUMENT-IDENTIFIER: US 5627024 A
TITLE: Lambdoid bacteriophage vectors for expression and display of foreign proteins

DEPR:
The use of the above particle segregation methods provides a means for screening a population of lambdoid phage particles present in a phage library of this invention. As applied to a phage library, screening can be utilized to enrich the library for one or more particles that express a multimer having a preselected substrate or ligand binding specificity. Where the library is designed to contain multiple species of multimers that all have some detectable measure of ligand binding activity, but differ in protein structure, ligand binding affinity or avidity, and the like, the screening methods can be utilized sequentially to first produce a library enriched for a preselected binding specificity, and then to produce a second library further enriched by further screening comprising one or more isolated phage particles. Methods for measuring ligand binding activities, and the like interactions between a ligand and a receptor are generally well known and are not discussed further as they are not essential features of the present invention.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 34. Document ID: US 5614361 A

L3: Entry 34 of 48 File: USPT Mar 25, 1997

US-PAT-NO: 5614361
DOCUMENT-IDENTIFIER: US 5614361 A

TITLE: Method for identifying and characterizing organisms

DATE-ISSUED: March 25, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Webster, Jr.; John A.	Springfield	VA	22152	N/A

US-CL-CURRENT: 435/5; 204/601, 204/614, 252/645, 435/6, 435/810, 536/23.1, 536/24.3, 536/24.32

ABSTRACT:

A method of characterizing an unknown organism species which comprises, determining the position of part or whole of evolutionarily conserved DNA sequences in DNA of the organism, relative to the position of restriction endonuclease cleavage sites in the DNA, thereby to obtain an identifying genetic characterization of the unknown organism, and comparing the characterization with information from at least two sets of identifying genetic characterizations derived from the same conserved sequences, each of the sets defining a known organism species.

11 Claims, 20 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 16

L3: Entry 34 of 48 File: USPT Mar 25, 1997

DOCUMENT-IDENTIFIER: US 5614361 A
TITLE: Method for identifying and characterizing organisms

DEPR:
A user can either compare the obtained characterization, e.g., band pattern, visually, or by aid of a one-dimensional, computer assisted, digital scanner programmed for recognition of patterns. These computer scanners are well known in the art of the time-of-sale transactions (the commonly utilized "supermarket" check-out pattern readers). Ideally, the library or catalog is present in a computer memory both in terms of the relative characterizations for a plurality of organisms, and in terms of the absolute values of molecular weight or size of the fragments. The catalog comparison then consists of matching the unknown characterization with one of the characterizations present in the library by means of either one or both of the stored information elements (relative characterizations and/or absolute size elements). The intensity of each band when compared to a standard can also reveal the amount of bound DNA hybridized, and thus can be used to estimate the extent of the presence of an organism, for example a prokaryote in a eukaryote. .

☐ 35. Document ID: US 5573905 A

L3: Entry 35 of 48 File: USPT Nov 12, 1996

US-PAT-NO: 5573905
DOCUMENT-IDENTIFIER: US 5573905 A

TITLE: Encoded combinatorial chemical libraries

DATE-ISSUED: November 12, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lerner; Richard	La Jolla	CA	N/A	N/A
Janda; Kim	San Diego	CA	N/A	N/A
Brenner; Sydney	Cambridge	N/A	N/A	GB2

US-CL-CURRENT: 435/6; 435/7.94, 435/DIG.21

ABSTRACT:

The present invention describes an encoded combinatorial chemical library comprised of a plurality of bifunctional molecules having both a chemical polymer and an identifier oligonucleotide sequence that defines the structure of the chemical polymer. Also described are the bifunctional molecules of the library, and methods of using the library to identify chemical structures within the library that bind to biologically active molecules in preselected binding interactions.

5 Claims, 2 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 2

L3: Entry 35 of 48 File: USPT Nov 12, 1996

DOCUMENT-IDENTIFIER: US 5573905 A
TITLE: Encoded combinatorial chemical libraries

BSPR:
In another embodiment, the invention contemplates a library comprising a plurality of species of bifunctional molecules, thereby forming a repertoire of chemical diversity.

DEPR:
An encoded combinatorial chemical library is a composition comprising a plurality of species of bifunctional molecules that each define a different chemical structure and that each contain a unique identifier oligonucleotide whose nucleotide sequence defines the corresponding chemical structure.

DEPR:
A library of this invention is a repertoire of chemical diversity comprising a plurality of species of bifunctional molecules according to the present invention. The plurality of species in a library defines a family of chemical diversity whose species each have a different chemical moiety. Thus the library can define a family of peptides, lipids, oligosaccharides or any of the other classes of chemical polymers recited previously.

DEPR:
The number of different species in a library represents the complexity of a library and is defined by the polymer length of the chemical moiety, and by the size of the chemical unit alphabet that can be used to build the chemical unit polymer. The number of different species referred to by the phrase "plurality of species" in a library can be defined by the formula V.sup.a, i.e., V to power of a (exponent a). V represents the alphabet size, i.e., the number of different chemical units X available for use in the chemical moiety. "a" is an exponent to V and represents the number of chemical units of X forming the polymer A, i.e., the length of polymer A.

☐ 36. Document ID: US 5523217 A

L3: Entry 36 of 48 File: USPT Jun 4, 1996

US-PAT-NO: 5523217
DOCUMENT-IDENTIFIER: US 5523217 A

TITLE: Fingerprinting bacterial strains using repetitive DNA sequence amplification

DATE-ISSUED: June 4, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lupski; James R.	Houston	TX	N/A	N/A
Koeuth; Thearith	Houston	TX	N/A	N/A
Versalovic; James	Houston	TX	N/A	N/A

US-CL-CURRENT: 435/91.2; 435/6, 536/24.32, 536/24.33

ABSTRACT:

Oligonucleotide primers and methods for identifying strains of bacteria by genomic fingerprinting are described. The methods are applicable to a variety of samples. The testing procedure includes amplifying the bacterial DNA in the sample to be tested by adding a pair of outwardly-directed primers to the sample. The primers are capable of hybridizing to repetitive DNA sequences in the bacterial DNA and extending outwardly from one hybridizable repetitive sequence to another hybridizable repetitive sequence. After amplification the extension products are separated by size and the specific strain of bacteria is determined by measuring the pattern of sized extension products. The procedure to identify strains of bacteria by fingerprinting has a variety of uses including: identifying bacteria in infections, agriculture and horticulture plots, bioremediation, food monitoring, production monitoring and quality assurance and quality control.

156 Claims, 17 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 17

L3: Entry 36 of 48 File: USPT Jun 4, 1996

DOCUMENT-IDENTIFIER: US 5523217 A
TITLE: Fingerprinting bacterial strains using repetitive DNA sequence amplification

CLPR:
22. The method of claim 1, wherein the sample contains a plurality of species of bacteria and wherein each specific species of bacteria is distinguished by comparing the size pattern of extension products to a library of known fingerprints to determine the identity of each specific species of bacteria in the sample.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw Desc | Image

☐ 37. Document ID: US 5512435 A

L3: Entry 37 of 48 File: USPT Apr 30, 1996

US-PAT-NO: 5512435
DOCUMENT-IDENTIFIER: US 5512435 A

TITLE: Receptor-binding antiproliferative peptides

DATE-ISSUED: April 30, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Renschler; Markus F.	Redwood City	CA	94063	N/A
Levy; Ronald	Stanford	CA	94043	N/A
Bhatt; Ramesh R.	Mountain View	CA	94025	N/A
Dower; William J.	Menlo Park	CA	94025	N/A

US-CL-CURRENT: 435/6; 435/5, 435/69.1, 435/965

ABSTRACT:

Methods and composition are provided for identifying antiproliferative polypeptides which inhibit clonal expansion and/or induce apoptosis in cells of a predetermined cell population (e.g., a neoplastic cell sample) expressing a cell surface receptor which is a member of the immunoglobulin superfamily. A predetermined cell population expressing surface immunoglobulin superfamily molecules is isolated from a patient as a cellular sample, such as a lymph node biospy or blood sample containing neoplastic lymphocytic cells. Antiproliferative peptides which are identified by the methods of the invention can be used as therapeutic agents for treating lymphoproliferative disorders by anti-idiotype therapy.

9 Claims, 3 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 3

L3: Entry 37 of 48 File: USPT Apr 30, 1996

DOCUMENT-IDENTIFIER: US 5512435 A
TITLE: Receptor-binding antiproliferative peptides

DEPR:
It has also been unexpectedly found that crosslinking anti-idiotype peptides, either by linking multiple molecules of a single species of anti-idiotype peptide or by linking multiple species of anti-idiotype peptides, results in enhanced biological activity for inhibiting proliferation, inducing clonal anergy, and/or inducing apoptosis in cells expressing cell surface immunoglobulin superfamily molecules of the characteristic idiotype used for screening the peptide library. Crosslinking is typically accomplished by synthesizing biotinylated anti-idiotype peptides and contacting them with streptavidin under aqueous binding conditions (e.g., buffered physiological saline, optionally including Tween and/or nonspecific blocking protein) to form crosslinked anti-idiotype peptides. Alternatively, anti-idiotype peptides may be crosslinked with a covalent crosslinking agent, such as 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (Pierce Chemical Co.) or succinimidyl 3-(2-pyridyldithio)propionate (Pierce Chemical Co.) according to methods described in the art (Gilliland et al. (1980) Proc. Natl. Acad. Sci. (U.S.A.) 77: 4539; Wu and Wu (1987) J. Biol. Chem. 262: 4429; Wu and Wu (1988) J. Biol. Chem. 263: 14621; Wu and Wu (1988) Biochemistry 27: 887; Wu et al. (1989) J. Biol. Chem. 264: 16985; Cotten et al. (1990) Proc. Natl. Acad. Sci. (U.S.A.) 87: 4033; Wagner et al. (1990) Proc. Natl. Acad. Sci. (U.S.A.) 87: 3410; Zenke et al. (1990) Proc. Natl. Acad. Sci. (U.S.A.) 87: 3655; and Wagner et al. (1991) Proc. Natl. Acad. Sci. (U.S.A.) 88: 4255, incorporated herein by reference. Peptides can be crosslinked through carboxy-terminal cysteines (e.g., which may be added carboxyterminal to a consensus sequence or substantially identical variant), typically using spacers such as bis-maleimidohexane (BMH) (Pierce Chemical Co.) which can covalently link two sulfhydryl groups. Preferably, crosslinking occurs at non-interfering positions so that substantial biological activity (e.g., antiproliferative activity) is retained. Such non-interfering positions generally are positions that do not form direct contacts with the immunoglobulin superfamily molecule(s) (e.g., surface IgM) to which the peptide or peptidomimetic binds to produce the therapeutic effect.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 38. Document ID: US 5348854 A

L3: Entry 38 of 48 File: USPT Sep 20, 1994

US-PAT-NO: 5348854
DOCUMENT-IDENTIFIER: US 5348854 A

TITLE: Method for detecting prokaryotic organisms

DATE-ISSUED: September 20, 1994

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Webster, Jr.; John A.	Billerica	MA	01821	N/A

US-CL-CURRENT: 435/6; 435/34, 435/810, 436/501, 436/504, 436/545, 436/804

ABSTRACT:

A method for detecting a prokaryotic organism while in the presence of or associated with a eukaryotic organism which comprises selectively hybridizing ribosomal RNA (rRNA) sequences of the prokaryotic organism with a detectably labelled prokaryotic rRNA information-containing hybridization probe; and detecting the label on the probe.

20 Claims, 20 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 16

L3: Entry 38 of 48 File: USPT Sep 20, 1994

DOCUMENT-IDENTIFIER: US 5348854 A
TITLE: Method for detecting prokaryotic organisms

DEPR:
A user can either compare the obtained band pattern visually, or by aid of a one-dimensional, computer assisted, digital scanner programmed for recognition of patterns. These computer scanners are well known in the art of the time-of-sale transact ions (the commonly utilized "supermarket" check-out pattern readers). Ideally, the library or catalog is present in a computer memory both in terms of the relative band patterns for a plurality of organisms, and in terms of the absolute values of molecular weight or size of the fragments. The catalog comparison then consists of matching the unknown pattern with one of the patterns present in the library by means of either one or both of the stored information elements (relative patterns and/or absolute size elements). The intensity of each band when compared to a standard can also reveal the amount of bound DNA hybridized, and thus can be used to estimate the extent of the presence of an organism, for example a prokaryote in a eukaryote.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 39. Document ID: US 5087558 A

L3: Entry 39 of 48 File: USPT Feb 11, 1992

US-PAT-NO: 5087558
DOCUMENT-IDENTIFIER: US 5087558 A

TITLE: Method for identifying and characterizing organisms

DATE-ISSUED: February 11, 1992

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Webster, Jr.; John A.	Springfield	VA	22152	N/A

US-CL-CURRENT: 435/5; 435/34, 435/4, 435/6, 435/810, 436/804, 536/24.3

ABSTRACT:

A method of characterizing an unknown organism species which comprises, determining the position of part or whole of evolutionarily conserved DNA sequences in DNA of the organism, relative to the position of restriction endonuclease cleavage sites in the DNA, thereby to obtain an identifying genetic characterization of the unknown organism, and comparing the characterization with information from at least two sets of identifying genetic characterizations derived from the same conserved sequences, each of the sets defining a known organism species.

43 Claims, 16 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 16

L3: Entry 39 of 48 File: USPT Feb 11, 1992

DOCUMENT-IDENTIFIER: US 5087558 A
TITLE: Method for identifying and characterizing organisms

DEPR:
A user can either compare the obtained characterization, e.g., band pattern, visually, or by aid of a one-dimensional computer assisted, digital scanner programmed for recognition of patterns. These computer scanners are well known in the art of the time-of-sale transactions (the commonly utilized "supermarket" check-out pattern readers). Ideally, the library or catalog is present in a computer memory both in terms of the relative characterizations for a plurality of organisms, and in terms of the absolute values of molecular weight or size of the fragments. The catalog comparison then consists of matching the unknown characterization with one of the characterizations present in the library by means of either one or both of the stored information elements (relative characterizations and/or absolute size elements). The intensity of each band when compared to a standard can also reveal the amount of bound DNA hybridized, and thus can be used to estimate the extent of the presence of an organism, for example a prokaryote in a eukaryote.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 40. Document ID: US 4885697 A

L3: Entry 40 of 48 File: USPT Dec 5, 1989

US-PAT-NO: 4885697
DOCUMENT-IDENTIFIER: US 4885697 A

TITLE: Method of identifying spectra

DATE-ISSUED: December 5, 1989

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hubner; Romeo J.	Wilmington	DE	N/A	N/A

US-CL-CURRENT: 702/27; 324/312, 356/303, 435/34

ABSTRACT:

A hierarchial library of spectra representing the point-by-point characteristics of known samples is created. Vectors representing each spectrum are classified according to their similarlity and dissimilarity. Vectors representing unknown samples are compared to known groups of vectors according to similarity until a near match is found.

20 Claims, 14 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 11

L3: Entry 40 of 48 File: USPT Dec 5, 1989

DOCUMENT-IDENTIFIER: US 4885697 A
TITLE: Method of identifying spectra

BSPR:
This photographic image contains a series of bands of varying widths and intensities along parallel linear paths corresponding to the gel electrophoresis lanes. This sheet is scanned with a standard CCD video camera to acquire an electronic image of the radiogram. This image has an appearance very much like a chromatogram containing peaks and valleys varying as a function of distance along the electrophoresis gel. This series of peaks and valleys is unique to the DNA which identifies a particular microorganism. Webster, Jr. suggests in his patent on column 15, line 24 that a user can either compare the obtained band pattern visually or by the aid of a one dimensional computer assisted digital scanner program for recognition of a pattern. The computer memory contains a library or catalog of the different band patterns for a plurality of known organisms. It is now simply a matter of comparing the unknown organism or pattern to the catalog of known patterns to achieve identity of the particular organism.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 41. Document ID: US 4717653 A

L3: Entry 41 of 48 File: USPT Jan 5, 1988

US-PAT-NO: 4717653
DOCUMENT-IDENTIFIER: US 4717653 A

TITLE: Method for identifying and characterizing organisms

DATE-ISSUED: January 5, 1988

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Webster, Jr.; John A.	Springfield	VA	22152	N/A

US-CL-CURRENT: 435/5; 435/35, 435/39, 435/6, 435/803, 436/501

ABSTRACT:

A method of characterizing an unknown organism which comprises comparing the chromatographic pattern of restriction endonuclease-digester DNA from the unknown organism, which digested DNA has been hybridized or reassociated with ribosomal RNA information-containing nucleic acid from or derived from a known probe organizm, with at least two equivalent chromatographic patterns, each one of the equivalent chromatographic patterns defining a known different organism species; and establishing the species of the unknown organism by means of a conserved set of ribosomal RNA sequence-containing restriction fragments present in the chromatographic pattern of the unknown organism.

41 Claims, 16 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 16

L3: Entry 41 of 48 File: USPT Jan 5, 1988

DOCUMENT-IDENTIFIER: US 4717653 A
TITLE: Method for identifying and characterizing organisms

DEPR:
A user can either compare the obtained band pattern visually, or by aid of a one-dimensional, computer assisted, digital scanner programmed for recognition of patterns. These computer scanners are well known in the art of the time-of-sale transactions (the commonly utilized "supermarket" check-out pattern readers). Ideally, the library or catalog is present in a computer memory both in terms of the relative band patterns for a plurality of organisms, and in terms of the absolute values of molecular weight or size of the fragments. The catalog comparison then consists of matching the unknown pattern with one of the patterns present in the library by means of either one or both of the stored information elements (relative patterns and/or absolute size elements). The intensity of each band when compared to a standard can also reveal the amount of bound DNA hybridized, and thus can be used to estimate the extent of the presence of a an organism, for example a prokaryote in a eukaryote.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 42. Document ID: US 5783431 A

L3: Entry 42 of 48 File: EPAB Jul 21, 1998

PUB-NO: US005783431A
DOCUMENT-IDENTIFIER: US 5783431 A
TITLE: Methods for generating and screening novel metabolic pathways

PUBN-DATE: July 21, 1998

INVENTOR-INFORMATION:

NAME	COUNTRY
PETERSON, TODD C	US
FOSTER, LYNDON M	US
BRIAN, PAUL	US

INT-CL (IPC): C12N 15/64; C07H 21/04

ABSTRACT:

The present invention relates to a novel drug discovery system for generating and screening molecular diversity. The system provides methods for mixing and cloning genetic materials from a plurality of species of organisms in combinatorial gene expression libraries to generate novel metabolic pathways and classes of compounds. The system also provides mobilizable combinatorial gene expression libraries that can be transferred from one species of host organism to another for expression. Also provided are specialized cloning vectors for making mobilizable gene expression libraries. The system also involves methods for pre-screening or identifying for host organisms containing a library that are capable of generating such novel pathways and compounds.

L3: Entry 42 of 48 File: EPAB Jul 21, 1998

DOCUMENT-IDENTIFIER: US 5783431 A
TITLE: Methods for generating and screening novel metabolic pathways

FPAR:
The present invention relates to a novel drug discovery system for generating and screening molecular diversity. The system provides methods for mixing and cloning genetic materials from a plurality of species of organisms in combinatorial gene expression libraries to generate novel metabolic pathways and classes of compounds. The system also provides mobilizable combinatorial gene expression libraries that can be transferred from one species of host organism to another for expression. Also provided are specialized cloning vectors for making mobilizable gene expression libraries. The system also involves methods for pre-screening or identifying for host organisms containing a library that are capable of generating such novel pathways and compounds.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 43. Document ID: WO 9826407 A2

L3: Entry 43 of 48 File: EPAB Jun 18, 1998

PUB-NO: WO009826407A2
DOCUMENT-IDENTIFIER: WO 9826407 A2
TITLE: DATABASE AND SYSTEM FOR STORING, COMPARING AND DISPLAYING GENOMIC INFORMATION

PUBN-DATE: June 18, 1998

INVENTOR-INFORMATION:

NAME	COUNTRY
SABATINI, CATHRYN E	N/A
HEATH, JOE DON	N/A
COVITZ, PETER A	N/A
KLINGER, TOD M	N/A
RUSSO, FRANK D	N/A
BERRY, STEPHANIE F	N/A

INT-CL (IPC): G11B 0/

ABSTRACT:

Disclosed is a relational database system for storing and manipulating biomolecular sequence information, the database including genomic libraries for a plurality of types of organisms, the libraries having multiple genomic sequences, at least some of which represent open reading frames located along a contiguous sequence on each the plurality of organisms' genomes, and a user interface capable of receiving a selection of two or more of the genomic libraries for comparison and displaying the results of the comparison. The system also provides a user interface capable of receiving a selection of one or more probe open reading frames for use in determining homologous matches between such probe open reading frame(s) and the open reading frames in the genomic libraries, and displaying the results of the determination.

L3: Entry 43 of 48 File: EPAB Jun 18, 1998

DOCUMENT-IDENTIFIER: WO 9826407 A2
TITLE: DATABASE AND SYSTEM FOR STORING, COMPARING AND DISPLAYING GENOMIC INFORMATION

FPAR:
Disclosed is a relational database system for storing and manipulating biomolecular sequence information, the database including genomic libraries for a plurality of types of organisms, the libraries having multiple genomic sequences, at least some of which represent open reading frames located along a contiguous sequence on each the plurality of organisms' genomes, and a user interface capable of receiving a selection of two or more of the genomic libraries for comparison and displaying the results of the comparison. The system also provides a user interface capable of receiving a selection of one or more probe open reading frames for use in determining homologous matches between such probe open reading frame(s) and the open reading frames in the genomic libraries, and displaying the results of the determination.

☐ 44. Document ID: WO 9817811 A1

L3: Entry 44 of 48 File: EPAB Apr 30, 1998

PUB-NO: WO009817811A1
DOCUMENT-IDENTIFIER: WO 9817811 A1
TITLE: METHODS FOR GENERATING AND SCREENING NOVEL METABOLIC PATHWAYS

PUBN-DATE: April 30, 1998

INVENTOR-INFORMATION:

NAME	COUNTRY
PETERSON, TODD C	N/A
FOSTER, LYNDON M	N/A
BRIAN, PAUL	N/A

INT-CL (IPC): C12N 15/64; C07H 21/04
EUR-CL (EPC): C12N015/10

ABSTRACT:

The present invention relates to a novel drug discovery system for generating and screening molecular diversity. The system provides methods for mixing and cloning genetic materials from a plurality of species of organisms in combinatorial gene expression libraries to generate novel metabolic pathways and classes of compounds. The system also provides mobilizable combinatorial gene expression libraries that can be transferred from one species of host organism to another for expression. Also provided are specialized cloning vectors for making mobilizable gene expression libraries. The system also involves methods for pre-screening or identifying for host organisms containing a library that are capable of generating such novel pathways and compounds.

L3: Entry 44 of 48 File: EPAB Apr 30, 1998

DOCUMENT-IDENTIFIER: WO 9817811 A1
TITLE: METHODS FOR GENERATING AND SCREENING NOVEL METABOLIC PATHWAYS

FPAR:
The present invention relates to a novel drug discovery system for generating and screening molecular diversity. The system provides methods for mixing and cloning genetic materials from a plurality of species of organisms in combinatorial gene expression libraries to generate novel metabolic pathways and classes of compounds. The system also provides mobilizable combinatorial gene expression libraries that can be transferred from one species of host organism to another for expression. Also provided are specialized cloning vectors for making mobilizable gene expression libraries. The system also involves methods for pre-screening or identifying for host organisms containing a library that are capable of generating such novel pathways and compounds.

☐ 45. Document ID: WO 9634112 A1

L3: Entry 45 of 48 File: EPAB Oct 31, 1996

PUB-NO: WO009634112A1
DOCUMENT-IDENTIFIER: WO 9634112 A1
TITLE: METHODS FOR GENERATING AND SCREENING NOVEL METABOLIC PATHWAYS

PUBN-DATE: October 31, 1996

INVENTOR-INFORMATION:

NAME	COUNTRY
THOMPSON, KATIE A	N/A
FOSTER, LYNDON M	N/A
PETERSON, TODD C	N/A

INT-CL (IPC): C12Q 1/04; C12Q 1/68; C12P 21/00; C07H 21/04; C12N 15/00
EUR-CL (EPC): C12N015/10

ABSTRACT:

The present invention relates to a novel drug discovery system for generating and screening molecular diversity. The system provides methods for mixing and cloning genetic materials from a plurality of species of organisms in combinatorial gene expression libraries to generate novel metabolic pathways and classes of compounds. The system also involves methods for pre-screening or identifying for host organisms containing a library that are capable of generating such novel pathways and compounds. The host organisms may be useful in drug screening for particular diseases, and in commercial production of compounds of interest. The methods of the invention are also useful in preserving the genomes of organisms that are known or prospective sources of drugs.

L3: Entry 45 of 48 File: EPAB Oct 31, 1996

DOCUMENT-IDENTIFIER: WO 9634112 A1
TITLE: METHODS FOR GENERATING AND SCREENING NOVEL METABOLIC PATHWAYS

FPAR:
The present invention relates to a novel drug discovery system for generating and screening molecular diversity. The system provides methods for mixing and cloning genetic materials from a plurality of species of organisms in combinatorial gene expression libraries to generate novel metabolic pathways and classes of compounds. The system also involves methods for pre-screening or identifying for host organisms containing a library that are capable of generating such novel pathways and compounds. The host organisms may be useful in drug screening for particular diseases, and in commercial production of compounds of interest. The methods of the invention are also useful in preserving the genomes of organisms that are known or prospective sources of drugs.

☐ 46. Document ID: WO 200109367 A1

L3: Entry 46 of 48 File: DWPI Feb 8, 2001

DERWENT-ACC-NO: 2001-182969
DERWENT-WEEK: 200118

TITLE: Determining nucleic acid sequences with the lowest rate of polymorphisms, useful as targets for developing drugs most likely to be effective and safe

INVENTOR: KELLY, C T; LEIGHTON, J ; SMITH, D ; THOMANN, H

PRIORITY-DATA: 1999US-0146003 (July 28, 1999)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 200109367 A1	February 8, 2001	E	029	C12P019/30

INT-CL (IPC): C12P 19/30

ABSTRACTED-PUB-NO: WO 200109367A
BASIC-ABSTRACT:

NOVELTY - Determining the nucleic acid sequence (S) of an endogenous gene in a population that has the lowest single-nucleotide variation among the population comprising:

(a) preparing a collection of genomic nucleic acids (NA) containing a portion of the endogenous genes of a population;

(b) determining the sequence polymorphisms (P) for NA; and

(c) determining S of NA which contain the lowest number of P, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) screening (M1) compounds (I) to identify drugs that target a region of an amino acid (aa) sequence with a reverse polymorphism rate (RPR);

(2) (I) identified by M1;

(3) ranking domains in a protein as potential drug targets by identifying RPR of an aa sequence or protein;

(4) a computer system (II) comprising:

(a) databases of genomic libraries for many organisms, each including multiple genomic and/or aa sequences, arranged as a reference sequence and related polymorphic sequences; and

(b) an interface that receives data for a new polymorphism and a display that ranks the new polymorphism to ascertain an RPR; and

(5) a computer program for (II).

USE - The sequence with the lowest frequency of polymorphisms in functional regions represents the best validated target site for development of drugs, especially those that modulate activity of a gene or protein.

ADVANTAGE - Drugs that target the region with lowest frequency of polymorphisms are likely to be effective and safe and to provide a uniform response among different ethnic groups.

L3: Entry 46 of 48 File: DWPI Feb 8, 2001

DERWENT-ACC-NO: 2001-182969
DERWENT-WEEK: 200118

TITLE: Determining nucleic acid sequences with the lowest rate of polymorphisms, useful as targets for developing drugs most likely to be effective and safe

ABTX:
(a) databases of genomic libraries for many organisms, each including multiple genomic and/or aa sequences, arranged as a reference sequence and related polymorphic sequences; and

☐ 47. Document ID: US 5970500 A, WO 9826407 A2, US 5966712 A

L3: Entry 47 of 48 File: DWPI Oct 19, 1999

DERWENT-ACC-NO: 1998-348778
DERWENT-WEEK: 199950

TITLE: Method of comparing genetic complement of different types of organism using relational database system - involves receiving selection of two or more of said sequence libraries for comparison by receiving user selection from two or more pull-down menus in graphical user interface

INVENTOR: BERRY, S F; COVITZ, P A ; HEATH, J D ; KLINGLER, T M ; RUSSO, F D ; SABATINI, C E ; KLINGER, T M

PRIORITY-DATA: 1997US-0857382 (May 15, 1997), 1996US-0032565 (December 12, 1996), 1997US-0856647 (May 15, 1997)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 5970500 A	October 19, 1999	N/A	000	G06F017/30
WO 9826407 A2	June 18, 1998	E	102	G11B000/00
US 5966712 A	October 12, 1999	N/A	000	G06F017/30

INT-CL (IPC): G06F 17/30; G11B 0/00

ABSTRACTED-PUB-NO: US 5966712A
BASIC-ABSTRACT:

The method involves providing a database including sequence libraries for a plurality of type of organisms. Said libraries has multiple bio-molecular sequences, which represent open reading frames located along contiguous sequences on each of the plurality of organisms' genomes. A selection of two or more of said sequence libraries is received for comparison. Open reading frames common or unique to the selected sequence libraries are determined. The database includes bio-molecular sequences from a microbial organism. The bio-molecular sequences include nucleic acid sequences and the nucleic acid sequences include genomic sequences. A selection of two or more of said sequence libraries are received for comparison which includes receiving a user selection from two or more pull-down menus in a graphical user interface.
ABSTRACTED-PUB-NO:

US 5970500A EQUIVALENT-ABSTRACTS:

The method involves providing a database including sequence libraries for a plurality of type of organisms. Said libraries has multiple bio-molecular sequences, which represent open reading frames located along contiguous sequences

sequences, which represent open reading frames located along contiguous sequences on each of the plurality of organisms' genomes. A selection of two or more of said sequence libraries is received for comparison. Open reading frames common or unique to the selected sequence libraries are determined. The database includes bio-molecular sequences from a microbial organism. The bio-molecular sequences include nucleic acid sequences and the nucleic acid sequences include genomic sequences. A selection of two or more of said sequence libraries are received for comparison which includes receiving a user selection from two or more pull-down menus in a graphical user interface.

The method involves providing a database including sequence libraries for a plurality of type of organisms. Said libraries has multiple bio-molecular sequences, which represent open reading frames located along contiguous sequences on each of the plurality of organisms' genomes. A selection of two or more of said sequence libraries is received for comparison. Open reading frames common or unique to the selected sequence libraries are determined. The database includes bio-molecular sequences from a microbial organism. The bio-molecular sequences include nucleic acid sequences and the nucleic acid sequences include genomic sequences. A selection of two or more of said sequence libraries are received for comparison which includes receiving a user selection from two or more pull-down menus in a graphical user interface.

WO 9826407A

L3: Entry 47 of 48 File: DWPI Oct 19, 1999

DERWENT-ACC-NO: 1998-348778
DERWENT-WEEK: 199950

TITLE: Method of comparing genetic complement of different types of organism using relational database system - involves receiving selection of two or more of said sequence libraries for comparison by receiving user selection from two or more pull-down menus in graphical user interface

ABTX:
The method involves providing a database including sequence libraries for a plurality of type of organisms. Said libraries has multiple bio-molecular sequences, which represent open reading frames located along contiguous sequences on each of the plurality of organisms' genomes. A selection of two or more of said sequence libraries is received for comparison. Open reading frames common or unique to the selected sequence libraries are determined. The database includes bio-molecular sequences from a microbial organism. The bio-molecular sequences include nucleic acid sequences and the nucleic acid sequences include genomic sequences. A selection of two or more of said sequence libraries are received for comparison which includes receiving a user selection from two or more pull-down menus in a graphical user interface.

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☐ 48. Document ID: US 6127190 A, WO 9618903 A1, ZA 9510550 A, AU 9643760 A, EP 797776 A1, US 5688696 A, AU 706091 B, IL 116360 A

L3: Entry 48 of 48 File: DWPI Oct 3, 2000

DERWENT-ACC-NO: 1996-300788
DERWENT-WEEK: 200050

TITLE: New combinatorial libraries, partic. for peptide(s) - having predetermined species of test cpds. on predetermined number of pieces of solid phase support

INVENTOR: LEBL, M

PRIORITY-DATA: 1994US-0354199 (December 12, 1994), 1997US-0971775 (November 17, 1997)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 6127190 A	October 3, 2000	N/A	000	G01N033/531
WO 9618903 A1	June 20, 1996	E	025	G01N033/543
ZA 9510550 A	August 28, 1996	N/A	024	C07K000/00
AU 9643760 A	July 3, 1996	N/A	000	G01N033/543
EP 797776 A1	October 1, 1997	E	000	G01N033/543
US 5688696 A	November 18, 1997	N/A	010	G01N033/531
AU 706091 B	June 10, 1999	N/A	000	G01N033/543
IL 116360 A	June 1, 2000	N/A	000	G01N033/543

INT-CL (IPC): C07K 0/00; G01N 33/531; G01N 33/543

L3: Entry 48 of 48 File: DWPI Oct 3, 2000

DERWENT-ACC-NO: 1996-300788
DERWENT-WEEK: 200050

TITLE: New combinatorial libraries, partic. for peptide(s) - having predetermined species of test cpds. on predetermined number of pieces of solid phase support

ABEQ:
A combinatorial library of multiple species of test cpds. comprises: (a) a predetermined number of separate solid phase supports, each support consisting of: (i) a single piece of a readily and continuously divisible matrix and (ii) a covalent linkage, and (b) a predetermined number of predefined species of test cpds. attached to the supports through the linkage. Each species comprises a predetermined number of subunits. The subunits occupy a predefined position, in which each species of test cpd. is attached to a predetermined number of supports and each support is attached to a single species of a test cpd.

ABEQ:
A combinatorial library of multiple species of test cpds. comprises: (a) a predetermined number of separate solid phase supports, each support consisting of: (i) a single piece of a readily and continuously divisible matrix and (ii) a covalent linkage, and (b) a predetermined number of predefined species of test cpds. attached to the supports through the linkage. Each species comprises a predetermined number of subunits. The subunits occupy a predefined position, in which each species of test cpd. is attached to a predetermined number of supports and each support is attached to a single species of a test cpd.

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